WHO Prequalification of In Vitro Diagnostics Programme
PUBLIC REPORT

Product: SD BIOLINE Malaria Ag P.f/P.v
Number: PQDx 0125-012-00

Abstract

SD BIOLINE Malaria Ag P.f/P.v with product code 05FK80 manufactured by Standard Diagnostics, Inc., CE marked regulatory version, was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 16 October 2015. This public report was amended 22 April 2016 to include SD BIOLINE Malaria Ag P.f/P.v with product codes 05FK83, 05FK86 and 05FK87.

SD BIOLINE Malaria Ag P.f/P.v test device contains a membrane strip, which is pre-coated with one monoclonal antibody and the other monoclonal antibody as two separate test lines across a test strip, a control line is also present.

One monoclonal antibodies (test line P.f) are specific to HRP-II of Plasmodium falciparum and the other monoclonal antibodies (test line P.v) are specific to the lactate dehydrogenase of P. vivax. This kit is intended for the detection of Malaria infection in human whole blood sample, indicating differential diagnosis between P.f HRP-II (Plasmodium falciparum, histidine-rich protein II) and pLDH (Plasmodium lactate dehydrogenase) specific to P. vivax. This kit is intended for professional use, only for an initial screening test and reactive samples should be confirmed by a supplemental assay such as microscopic examination of thin blood smear.

SD BIOLINE Malaria Ag P.f/P.v test is a rapid, qualitative immunochromatographic test for the differential detection of HRP-II (Histidine-rich protein II) specific to P. falciparum and pLDH (Plasmodium lactate dehydrogenase) specific to P. vivax in human whole blood.

As with all diagnostic tests, a definitive clinical diagnosis should not be based on the results of a single test results, but should only be made by the physician after all clinical and laboratory findings have been evaluated.

<table>
<thead>
<tr>
<th>Test cassettes</th>
<th>25T/kit (product code 05FK80)</th>
<th>1T/kit x 25ea (product code 05FK83)</th>
<th>10T/kit (product code 05FK86)</th>
<th>25T/kit (product code 05FK87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>individually packed in foil pouch with a desiccant</td>
<td>25 test devices</td>
<td>25x 1 test device</td>
<td>10 test devices</td>
<td>25 test devices (in 3 kits; 2 kits containing 8T/kit)</td>
</tr>
</tbody>
</table>
Assay diluent
dispensed in plastic bottle

<table>
<thead>
<tr>
<th>Component</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assay diluent</td>
<td>1 x 5ml/bottle</td>
</tr>
<tr>
<td>Specimen transfer devices</td>
<td>25x 180µl/vial</td>
</tr>
<tr>
<td>Specimen transfer devices</td>
<td>1 x 3ml/bottle</td>
</tr>
<tr>
<td>Specimen transfer devices</td>
<td>3 x 5ml/bottle</td>
</tr>
<tr>
<td>Specimen transfer devices</td>
<td>10 units of 5µl</td>
</tr>
<tr>
<td>Specimen transfer devices</td>
<td>30 units of 5µl</td>
</tr>
<tr>
<td>Specimen transfer devices</td>
<td>25 units</td>
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<tr>
<td>Specimen transfer devices</td>
<td>10 units</td>
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<tr>
<td>Specimen transfer devices</td>
<td>30 units</td>
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<td>Specimen transfer devices</td>
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<td>Specimen transfer devices</td>
<td>10 units</td>
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<tr>
<td>Specimen transfer devices</td>
<td>30 units</td>
</tr>
<tr>
<td>Alcohol swabs (optional)</td>
<td>25 units</td>
</tr>
<tr>
<td>Alcohol swabs (optional)</td>
<td>10 units</td>
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<tr>
<td>Alcohol swabs (optional)</td>
<td>30 units</td>
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<td>Alcohol swabs (optional)</td>
<td>25 units</td>
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<tr>
<td>Alcohol swabs (optional)</td>
<td>10 units</td>
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<td>Alcohol swabs (optional)</td>
<td>30 units</td>
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<td>Alcohol swabs (optional)</td>
<td>25 units</td>
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<tr>
<td>Alcohol swabs (optional)</td>
<td>10 units</td>
</tr>
<tr>
<td>Alcohol swabs (optional)</td>
<td>30 units</td>
</tr>
<tr>
<td>Assay diluent</td>
<td>1 copy</td>
</tr>
<tr>
<td>Assay diluent</td>
<td>1 copy</td>
</tr>
<tr>
<td>Assay diluent</td>
<td>1 copy</td>
</tr>
<tr>
<td>Assay diluent</td>
<td>6 copies</td>
</tr>
<tr>
<td>Summary instructions</td>
<td>N/A</td>
</tr>
<tr>
<td>Summary instructions</td>
<td>25 copies</td>
</tr>
<tr>
<td>Summary instructions</td>
<td>N/A</td>
</tr>
<tr>
<td>Summary instructions</td>
<td>N/A</td>
</tr>
</tbody>
</table>

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

Shelf-life:
24 months.

Summary of prequalification status for SD BIOLINE Malaria Ag P.f/P.v

<table>
<thead>
<tr>
<th>Component</th>
<th>Initial acceptance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Date</td>
</tr>
<tr>
<td>PQ status amended</td>
<td>22 April 2015 and 2 May 2016</td>
</tr>
<tr>
<td>Status on PQ list</td>
<td>16 October 2015</td>
</tr>
<tr>
<td>Dossier assessment</td>
<td>14 August 2015</td>
</tr>
<tr>
<td>Inspection status</td>
<td>24 July 2015</td>
</tr>
<tr>
<td>Laboratory evaluation</td>
<td>Round 2 (2009) and Round 6 (2015)</td>
</tr>
</tbody>
</table>

MR: Meets Requirements
NA: Not Applicable

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

Background information
Standard Diagnostics, Inc., submitted an application for prequalification SD BIOLINE Malaria Ag P.f/P.v. Based on the results of the WHO product testing of malaria RDTs Round 2, SD BIOLINE Malaria Ag P.f/P.v was given priority for prequalification.

Product dossier assessment

Standard Diagnostics, Inc., submitted a product dossier for SD BIOLINE Malaria Ag P.f/P.v 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/P.v for prequalification.

Commitments for prequalification:
The manufacturer committed to amend and submit additional documentation on the following issues:
2. The manufacturer also commits to seek specimens from patients infected with Schistosoma to test for possible cross-reactions.

Manufacturing site inspection

A comprehensive inspection was performed at the site of 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) of SD BIOLINE Malaria Ag P.f/P.v in May 2015 as per the Information for manufacturers on prequalification inspection procedures for the sites of manufacture of diagnostics (PQDx_014 v1). The inspection found that the manufacturer had an acceptable quality management system and good manufacturing practices in place that ensured the consistent manufacture of a product of good quality. The manufacturer's responses to the nonconformities found at the time of the inspection were accepted 24 July 2015.

Commitments for prequalification:
N/A

Laboratory evaluation

The product was evaluated in Round 2 and Round 6 of WHO/FIND product testing of RDTs for malaria antigen detection was completed in 2009 and 2015. 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 P. falciparum negative panel. Thermal

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1 Previous site inspections were carried out in September 2010, March 2012, and November 2012.
stability was assessed after 2 months of storage at elevated temperature and humidity, and a descriptive ease of use assessment was recorded.

For Round 2, the following results were observed: *P. falciparum* panel detection score (96.0% at 200 parasites/μl), *P. vivax* panel detection score (95.0% at 200 parasites/μl), false-positive rates (3.5% for clean negatives, 0% for *P. falciparum* at 200 parasites/μl, 0% for *P. vivax* at 200 parasites/μl, 100% for *P. falciparum* at 2000 or 5000 parasites/μl, 100% for *P. vivax* at 2000 or 5000 parasites/μl) and invalid rate (0.2%).

For Round 6, the following results were observed: *P. falciparum* panel detection score (92.0% at 200 parasites/μl), *P. vivax* panel detection score (94.30% at 200 parasites/μl), false-positive rates (1.9% for clean negatives, 0.5% for *P. falciparum* at 200 parasites/μl, 0.7% for *P. vivax* at 200 parasites/μl, 100% for *P. falciparum* at 2000 or 5000 parasites/μl, 100% for *P. vivax* at 2000 or 5000 parasites/μl) and invalid rate (0.2%).

<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></td>
<td>Pf</td>
<td>Pv</td>
<td>Clean negatives</td>
</tr>
<tr>
<td>Round 2</td>
<td>96.0</td>
<td>95.0</td>
<td>0</td>
</tr>
<tr>
<td>Round 6</td>
<td>92.0</td>
<td>94.3</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Therefore, SD BIOLINE Malaria Ag P.f/P.v meets the current laboratory evaluation requirements for prequalification.

**Change notification**

In 2015, Standard Diagnostics, Inc., submitted three change notifications related to:

1. Re-introduction of a stable single-use buffer vial (for product code 05FK83).
2. Different packaging configuration for the test kit (for product code 05FK86, 05FK87).
3. Changes to the labelling of the cassette (for product codes 05FK80, 05FK83, 05FK86, 05FK87).

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 05FK80
1.2 Foil pouch for test cassettes of 05FK80
1.3 Package box for 05FK83 [POCT]
1.4 Outer pouch for 05FK83 [POCT]
1.5 1-test foil pouch for test cassettes of 05FK83 [POCT]
1.6 Package box for 05FK86
1.7 Package box for 05FK87 (25T)
1.8 Package box for 05FK87 (8T)
1.9 Package box for 05FK87 (9T)
1.10 Foil pouch for test cassettes of 05FK86, 05FK87
2. Instructions for use

2.1 IFU for 05FK80
2.2 IFU for 05FK83 [POCT]
2.3 Summarized IFU for 05FK83 [POCT]
2.4 IFU for 05FK86

![One Step Malaria P. falciparum and P. vivax Antigen Rapid Test](image)

**About the test**

Introduces the test and explains that the test is a rapid test for detecting malaria caused by Plasmodium falciparum and Plasmodium vivax. The test is a one-step, qualitative, lateral flow immunoassay that uses the P. falciparum and P. vivax antigens to detect the presence of malaria in a single drop of blood. The test requires minimal sample preparation and is easy to perform. The test results are read visually, and the test line appears within 10 minutes.

**Internal quality control**

The test includes a positive control (P) and a negative control (N) to ensure the test's accuracy. The positive control should show a single line, while the negative control should show no line. If either control line is not visible, the test result should be considered invalid.

**Expected results**

The test results should be interpreted based on the presence of a test line (T) and a control line (C). The following interpretations are expected:

- **Negative**: Both C and T lines are present, indicating no malaria infection.
- **Positive**: Only the T line is present, indicating a positive malaria infection.

**Performance characteristics**

<table>
<thead>
<tr>
<th>Test Line (T)</th>
<th>Control Line (C)</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>100%</td>
<td>99.5%</td>
<td>99.5%</td>
</tr>
</tbody>
</table>

**Materials provided and active ingredients of main components**

- Test device: Malaria Ag Pf/Pv (05FK86)
- Sample collector (bone marrow, blood)
- Control solution (positive and negative)
- Adhesive strip
- Protective cover
- Instruction manual

**Materials required but not provided**

- Monophasic reagent
- Disposable container

**Kit storage and stability**

- Store at room temperature (15°C to 25°C) for up to 12 months.
- Do not freeze or refrigerate the kit components.
- Use within the specified shelf life.

**Warnings**

- Do not use if the test is expired or damaged.
- Do not use for any other indication than malaria.
- Do not use on patients with a known sensitivity to the test ingredients.
- Do not use on patients with a known history of malaria.

**Specimen collection and storage**

- Collect a blood or bone marrow sample from the patient.
- Store the sample at room temperature until testing.
- Use within 24 hours of collection.

**Test procedures (before to figure)**

1. Collect a blood or bone marrow sample from the patient.
2. Keep the sample at room temperature until testing.
3. Perform the test according to the instructions.
4. Read the results visually after 10 minutes.

**Test interpretation (before figure)**

- **Positive**: Single line (T) only, indicating malaria infection.
- **Negative**: Both lines (T and C) present, indicating no malaria infection.

**Limitations and interferences**

- The test may be affected by the presence of certain drugs or by the patient's immune response.
- The test may not detect malaria in asymptomatic individuals or in early stages of infection.

**Bibliography of suggested reading**

1. CDC. Malaria. Available at: [CDC.gov](https://www.cdc.gov/malaria)
2. WHO. Malaria. Available at: [WHO.org](https://www.who.int/malaria)
3. CDC. Laboratory supportive criteria for diagnosis of malaria. Available at: [CDC.gov](https://www.cdc.gov/malaria/diagnosis-treatment/lab-support.html)
4. WHO. Laboratory diagnosis of malaria. Available at: [WHO.org](https://www.who.int/malaria/diagnosis-treatment/lab-diagnosis.html)
Test procedure

1. Open the package and look for the following:
   1. Test card
   2. Alcoholic swab
   3. Paper wipe

2. First, carefully read the instructions for using the SD BOXIN Malaria Ag Pf/Pv test kit.

3. Next, look at the expiration date on the back of the test card. If the expiration date has passed, do not use the test kit.

4. Open the test pack and follow the instructions:
   1. Place the test strip on a flat surface.
   2. Add 10 drops of blood to the test strip.
   3. Place the test strip in the testing device.

5. After 15 minutes, interpret the results:
   - **Negative**: No lines in the result windows.
   - **Positive**: At least 1 line in the result windows. It is recommended that the test be confirmed using a different method.

6. Dispose of the test strip and testing device.

Interpretation

- **Negative**
  - No malaria/Pf/Pv infection

- **Positive**
  - Two colored lines (test line “Pf” and control line “C”)
  - Caution: It is positive even if “Pf” line is blist.
2.5 IFU for 05FK87