WHO Prequalification of In Vitro Diagnostics
PUBLIC REPORT

Product: Bioline HBsAg WB
WHO reference number: PQDx 0219-012-00

Bioline HBsAg WB with product code 01FK10W, manufactured by Abbott Diagnostics Korea Inc\(^2\), Rest-of-World (RoW) regulatory version, was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 22 December 2017.

### Summary of WHO prequalification assessment for Bioline HBsAg WB

<table>
<thead>
<tr>
<th>Date</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>PQ listing</td>
<td>22-Dec-2017 listed</td>
</tr>
<tr>
<td>Dossier review</td>
<td>18-Sep-2017 MR</td>
</tr>
<tr>
<td>Site inspection(s) of quality management system</td>
<td>26 – 29-Jun-2017 MR</td>
</tr>
<tr>
<td>Product performance evaluation</td>
<td>10-Nov-2016 MR</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Version</th>
<th>Summary of amendment</th>
<th>Date of report amendment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 to 3.0</td>
<td>Changes to the draft public report before listing.</td>
<td>22-Dec-2016</td>
</tr>
<tr>
<td>4.0</td>
<td>Product name was changed from SD BIOLINE HBsAg WB to Bioline HBsAg WB. Manufacturer’s name changed from Standard Diagnostics Inc to Abbott Diagnostics Korea Inc.</td>
<td>20-Aug-2020</td>
</tr>
</tbody>
</table>

---

1 Product name was changed from SD BIOLINE HBsAg WB to Bioline HBsAg WB.
2 Manufacturer’s name changed from Standard Diagnostics Inc to Abbott Diagnostics Korea Inc
Intended use:

According to the claim of intended use from Abbott Diagnostics Korea Inc, “Bioline HBsAg WB is an in vitro immunochromatographic, rapid assay designed for the qualitative detection of Hepatitis B surface antigen, in human serum, plasma (heparin, EDTA and sodium citrate) or venous whole blood (heparin, EDTA and sodium citrate). Bioline HBsAg WB is intended only for professional use as an aid to diagnosis. Reactive specimens should be reflexed for additional testing, either by Enzyme immunoassay (EIA) to identify current HBV infection. This product is intended for use in a population with high HBV prevalence. This test may not be suitable for diagnosis of early infection or blood donation screening. Because false non-reactive results may also arise due to the lack of ability of the assay to detect HBsAg mutants. The performance of Bioline HBsAg WB in infants or children has not been validated.”

Assay description:

According to the claim of assay description from Abbott Diagnostics Korea Inc, “the membrane is pre-coated with mouse monoclonal anti-HBsAg pool on the test line region and Mouse monoclonal anti-chicken IgY on the control line region. During testing, the specimen is allowed to react with the colored conjugate (mouse monoclonal anti-HBsAg conjugated gold colloid) which was pre-coated on the test strip. The mixture (mouse monoclonal anti-HBsAg + HBsAg in specimen) then moves upward on the membrane chromatographically by capillary action. For a reactive result, a purple colored line with the antibody-antigen-antibody gold particle complex will form in the test line region of the result window. An absence of this purple-colored line in the test line region suggests a non-reactive result. Regardless of the presence of HBsAg, chicken IgY conjugated gold colloid, pre-coated on the test strip, continues to move across the membrane to immobilized mouse monoclonal anti-chicken IgY, then a purple-colored line at the control line region of the result window appears. The presence of a purple colored line in the control line region serves as 1) verification that sufficient volume of specimen has been added and 2) that proper flow has been obtained.”

Test kit contents:

<table>
<thead>
<tr>
<th>Component</th>
<th>30 tests (product code 01FK10W)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test device:</td>
<td>30</td>
</tr>
<tr>
<td>With desiccant in an individual foil pouch.</td>
<td>30</td>
</tr>
<tr>
<td>Instructions for use</td>
<td>1</td>
</tr>
</tbody>
</table>
Items required but not provided:

<table>
<thead>
<tr>
<th>Item</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Consumables:</strong></td>
</tr>
<tr>
<td>Gloves</td>
</tr>
<tr>
<td><strong>Durables:</strong></td>
</tr>
<tr>
<td>N/A</td>
</tr>
<tr>
<td><strong>Equipment:</strong></td>
</tr>
<tr>
<td>Micropipette</td>
</tr>
<tr>
<td>Timer</td>
</tr>
<tr>
<td>Biohazard disposal container</td>
</tr>
</tbody>
</table>

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

Shelf-life upon manufacture:
24 months.

Warnings/limitations:
See manufacturer’s instructions for use.

Prioritization for prequalification
Based on the established eligibility criteria, Bioline HBsAg WB was given priority for WHO prequalification assessment.

Product dossier assessment

Abbott Diagnostics Korea Inc. submitted a product dossier for Bioline HBsAg WB as per the “Instructions for compilation of a product dossier” (PQDx_018 v1). 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 screening and assessment findings were accepted on 18 September 2017.

Commitments for prequalification:

Commitment for prequalification:

The double reading legend will be removed from the cassette. The change will be implemented in Q2-2018. The updated documentation in relation to this change should be submitted in Q2-2018 or as soon as the change is applied.
WHO will to follow-up on implementation of this commitment at the next re-inspection.

Based on the product dossier screening and assessment findings, the product dossier for Bioline HBsAg WB meets WHO prequalification requirements.

### Manufacturing site inspection

A comprehensive inspection was performed at the site(s) of manufacture (65, Borahagal-ro, Giheung-gu, Yongin-si, Gyeonggi-do and 46 Hagal-ro 15beon-gil, Giheung-gu, Yongin-si, Gyeonggi-do) of Bioline HBsAg WB in 26-29 June 2017 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 would, once the commitments to WHO are fulfilled, ensure 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 on 19 December 2017.

**Commitments for prequalification:**

1. Certain process validations to be completed, and applicable production documentation to be updated by June 2018.
2. Stability studies to be performed using samples from routine production batches.
3. Evidence to be provided that the performance of lots submitted for WHO laboratory performance evaluation are equivalent to the performance of routinely manufactured batches by June 2018.

Confirmation of implementation of these commitments will be followed-up at re-inspection.

Based on the site inspection and corrective action plan review, the quality management system for Bioline HBsAg WB meets WHO prequalification requirements, subject to fulfillment of the above commitments.

### Manufacturing site inspection

Bioline HBsAg WB is a lateral flow immunochromatographic rapid diagnostic test for the detection of HBsAg in human serum, plasma or whole blood. A volume of 100μL of specimen is needed to perform the assay. This type of assay requires no sophisticated equipment and can therefore be performed in laboratories with limited facilities. Reading of the results can be done visually.
In this limited evaluation on a panel of 514 specimens, we found an initial sensitivity (95% CI of 100% (98.1% – 100%)) and an initial specificity (95% CI) of 98.7% (96.8% – 99.7%) compared to the reference assays. The final sensitivity (95% CI) was 100% (98.1% – 100%) and the final specificity (95% CI) was 99.0% (97.2% – 99.8%) compared to the reference assays. The lot to lot variability was acceptable.

<table>
<thead>
<tr>
<th>Performance characteristics in comparison with an agreed reference standard</th>
<th>Initial (95% CI)</th>
<th>Final (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity %</td>
<td>100% (98.1 – 100%)</td>
<td>100% (98.1 – 100%)</td>
</tr>
<tr>
<td>Specificity %</td>
<td>98.7% (96.8 – 99.7%)</td>
<td>99.0% (97.2 – 99.8%)</td>
</tr>
<tr>
<td>Invalid rate %</td>
<td>0.2%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Inter-reader variability %</td>
<td>0.2%</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Additional performance characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity during seroconversion on 6 seroconversion panels in comparison with a benchmark assay; Monolisa Ag HBs Plus (bio-Rad)</td>
<td>Seroconversion sensitivity index of +2, therefore detection is 2 days later than the benchmark assay</td>
</tr>
<tr>
<td>Analytical sensitivity on a HBsAg low titer panel in comparison with an agreed reference standard</td>
<td>0 of 14 specimens were correctly classified.</td>
</tr>
<tr>
<td>Analytical sensitivity on WHO International Biological Reference Preparation for HBsAg</td>
<td>2.06 IU/ml</td>
</tr>
<tr>
<td>Lot to lot variation on a dilution panel in comparison with an agreed reference standard</td>
<td>Acceptable</td>
</tr>
<tr>
<td><strong>Key operational characteristics</strong></td>
<td></td>
</tr>
<tr>
<td>-------------------------------------</td>
<td>--------------------------------</td>
</tr>
<tr>
<td>Validated specimen types</td>
<td>Serum, plasma (heparin, EDTA and sodium citrate), venous whole blood</td>
</tr>
<tr>
<td>Number of steps</td>
<td>1 with precision required</td>
</tr>
<tr>
<td>Time to result</td>
<td>20 minutes</td>
</tr>
<tr>
<td>Endpoint stability</td>
<td>0 minutes (must be read immediately after 20 minutes)</td>
</tr>
<tr>
<td>Internal QC</td>
<td>Yes, reagent addition only</td>
</tr>
<tr>
<td>In-use stability of reagents</td>
<td>Use immediately</td>
</tr>
</tbody>
</table>
Labelling

1. Labels
2. Instructions for use

*Note: Labelling has been changed as per site name change and product rebranding. But temporarily labelling of legacy brand (SD BIOLINE) will be used in the market according to registration status in each country.
1. Labels

1.1 Package box for 01FK10W
1.2 Device pouch for 01FK10W
2. Instructions for use

---

3 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.
• Non-reactive result:

3. Using a micropipette, dispense 100µl of serum, plasma or whole blood specimen into the specimen

1. Bring the test device and specimen to a temperature between 15 - 40 °C prior to testing.

• Using venipuncture, draw whole blood and insert it into the collection tube (containing

1. The test kit should be stored at a temperature between 1 °C and 40 °C. Do not freeze the kit or its

components.

Serum to plasma equivalence is demonstrated on 25 positive and 25 negative serum / EDTA

samples from patients were screened with Bioline™ HBsAg WB as well as with

HBsAg confirmation assay (Abbott). In two samples the Bioline™ HBsAg WB obtained a non-

reactive result.

Even though our intended performance is as above, the results of individual laboratories may vary

in six different seroconversion panels (PMH903, PHM907, PHM910, PHM916, PHM928 and

PMH914) Panel de preparación de referencia de la OMS

Aucun des échantillons mutants d’antigène HBsAg issus du panel de DiaSorin n’a obtenu de

résultats non-reactionnels false positivos. La spécificité de 100 % (IC à 95 % : 99,5 - 100 %).

Les 514 échantillons dérivés cliniquement d’échantillons de sérum/plasma venant d’Europe,

les échantillons provenaient de 2 sites de prélèvement en Allemagne, à Francfort et à

Londres. Les 100 échantillons de patients HBeAg positifs ont été testés. Les 100 ensembles d’échantillons de sang total et de plasma positifs à l’antigène HBsAg ont été

testées dans le laboratoire de biologie clinique de l’hôpital universitaire de Sanquin à Amsterdam.

Les échantillons de sérum/plasma de 362 patients infectés par le virus de l’hépatite B au cours

de l’année 1987 à l’hôpital universitaire de Sanquin à Amsterdam ont été testés. Les résultats des

échantillons cliniques ont été comparés aux résultats des tests de laboratoire de la

Cruz Vermelha alemã. O Bioline™ HBsAg WB foi positivo em todas as 100 amostras

estas limitações no caso dos testes IVD qualitativos, uma linha de teste pode ser ténue ou

aparecer uma linha de color púrpura em torno da membrana lida no exterior do pino de controle. A

linha de teste deve ser claramente visível para só considerar o resultado como positivo.

Bioline™ HBsAg WB

- Conjugados de ouro: ouro coloidal conjugado com anti-HBsAg monoclonal de ratinho

- Anti-HBs: IgY de galinha conjugado com ouro colloidal

2. As instruções devem ser seguidas com exatidão para obter resultados precisos. Qualquer indivíduo

in vitro.

- Ante la prueba, lleve el dispositivo de prueba y la muestra a temperatura ambiente (entre 15 °C y

90 °C) para que la prueba esté funcionando correctamente.

- Limpie cualquier derrame con un desinfectante adecuado.

- No reutilice el dispositivo de prueba una vez utilizado, y no lo someta a ciclos repetidos de

congelación y descongelación.

- Limite la prueba al envase de uno de las pruebas in vitro.

- El dispositivo de prueba no debe ser utilizado por individuos que no tengan experiencia con su

usar este tipo de prueba in vitro.

2. The device is sensitive to humidity and temperature. Perform the test immediately and avoid

limiting exposure to test conditions. Never re-use the test device.

2. Each of the 12 potential agents of infection that could cross-react with HBsAg were tested with the Bioline™ HBsAg WB.

No reutilizar el dispositivo de prueba una vez utilizado, y no lo someta a ciclos repetidos de

congelación y descongelación.

2. The test kit should be stored at a temperature between 1 °C and 40 °C. Do not freeze the kit or its

components.

Aucun des échantillons mutants d’antigène HBsAg issus du panel de DiaSorin n’a obtenu de

résultats non-reactionnels false positivos. La spécificité de 100 % (IC à 95 % : 99,5 - 100 %).

Estudo 2: Avaliação de laboratório da OMS

Los siguientes 12 potenciales agentes patogénicos con reatividade cruzada no tiveram qualquer

incidence sur les résultats du test Bioline™ HBsAg WB.

Limitations of the test described in these Instructions for Use.

3. Therefore, it is possible that non-reactive false positive results may occur. These limitations

are limited. Por este motivo, es posible que se generen resultados no reactivos falsos. Estas limitaciones

in vitro.

resultado obtido pelo Bioline™ HBsAg WB foi integralmente positivo.

Capítulo 1: Introdução

Equipo de prueba

3. Precauciones

Aunque este ensayo ha demostrado ser capaz de detectar genotipos de HBsAg en las muestras de

de la prueba debe ser un especialista capacitado para usarlo.

3. Ingredients ativo de los componentes principales

O teste Bioline™ HBsAg WB demonstrou que até 23.000 IU/mL de HBsAg não apresenta efeito

in vitro. No total, 43 amostras foram positivas com o teste Bioline™ HBsAg WB e 96 amostras foram

negativas.

Estudo 1: Curva de sensibilidade e especificidade

Les 514 échantillons dérivés cliniquement d’échantillons de sérum/plasma venant d’Europe,

Les 12 agents pathogènes suivants susceptibles de provoquer une réactivité croisée n’ont eu aucune

réaction positive avec le test Bioline™ HBsAg WB. Les échantillons de sérum/plasma de

les échantillons provenaient de 2 sites de prélèvement en Allemagne, à Francfort et à

Londres. Les 100 échantillons de patients HBeAg positifs ont été testés. Les 100 ensembles d’échantillons de sang total et de plasma positifs à l’antigène HBsAg ont été

testées dans le laboratoire de biologie clinique de l’hôpital universitaire de Sanquin à Amsterdam.

Les échantillons de sérum/plasma de 362 patients infectés par le virus de l’hépatite B au cours

de l’année 1987 à l’hôpital universitaire de Sanquin à Amsterdam ont été testés. Les résultats des

échantillons cliniques ont été comparés aux résultats des tests de laboratoire de la

Cruz Vermelha alemã. O Bioline™ HBsAg WB foi positivo em todas as 100 amostras

Negativos a 90.000 IU/mL de HBsAg.

After 30 minutes, examine the test results. A positive result is indicated by the appearance of a

color line in the test line area of the test result section. If the test result area shows no color line

at all, the test is considered valid. If a line of color appears in the control line area, but not in the

test line area, the test is considered invalid. If both control and test lines appear, the test is

considered invalid. If the test device is functioning correctly, the test result area should appear as

shown in the image.
TEST PROCEDURE / PROCÉDURE DE TEST / PROCEDIMIENTO DE LA PRUEBA / PROCEDIMENTO DO TESTE

Specimen collection / Prélèvement de l’échantillon / Obtención de la muestra / Coleta de amostras

1. Take 100 μl of serum, plasma or whole blood specimen using a syringe and a needle. (Dispense 100 μl of serum, plasma or whole blood specimen into the specimen well “S”)

2. Prélèver 100 μl d’échantillon de sérum, de plasma ou de sang total dans le poço d’échantillon “S”

3. Con un micropipeta, tome 100 μl de la muestra de suero, plasma o sangre

4. Instile 100 μl of serum, plasma or whole blood into the specimen well “S”.

INTERPRETATION / INTERPRÉTATION / INTERPRETACIÓN / INTERPRETAÇÃO

NON-REACTIVE / NON RÉACTIF / NO REACTIVO / NÃO REATIVO

- If the control line (C) and the test line (T) are not visible in the result window, regardless of the color of the lines, the result is considered non-reactive.

- If only the control line (C) is visible in the result window, the result is considered non-reactive.

REACTIVE / RÉACTIF / REACTIVO / REATIVO

- If either the test line (T) or the control line (C) is visible in the result window, the result is considered reactive.

INVALID / NON VALIDE / NO VÁLIDO / INVALIDA

- If the control line (C) is visible in the result window, the result is considered invalid.

Preparation / Préparation / Preparación / Preparação

1. Open the package and look for the following:
   - 1 Test device with desiccant and an identification label
   - Instructions for use

2. Carefully read the instructions for using the Bioline® HBsAg WB test.

3. Place the specimen on the test device.

4. Open the test device and follow the following:
   - 1 Test device with desiccant
   - 2 Dispersant

5. Add 100 μl of specimen into the specimen well “S”.

6. Interpret test results at 20 minutes. Do not read test results after 20 minutes, late readings can yield false results.

7. Interpret the results of the test at least 20 minutes. The test results are valid for a period of 20 minutes, after which time the test may yield false results.

8. Interpret test results after 20 minutes. False positive results are possible.

9. The test results obtained within 20 minutes, the letters and numbers can generate false results.

10. Interpret the results of the test within 20 minutes. False results are possible.

11. Interpret test results at 20 minutes. False results are possible.

PREPARATION / PRÉPARATION / PREPARACIÓN / PREPARAÇÃO

1. Open the package and identify the following elements:
   - 1 Test device with desiccant
   - 2 Dispensers
   - 2 Instructions for use

2. Open the package and identify the following elements:
   - 1 Test device with desiccant
   - 2 Dispensers
   - 2 Instructions for use

3. Open the package and identify the following elements:
   - 1 Test device with desiccant
   - 2 Dispensers
   - 2 Instructions for use

4. Carefully read the instructions for using the Bioline® HBsAg WB test.

5. Carefully read the instructions for using the Bioline® HBsAg WB test.

6. Carefully read the instructions for using the Bioline® HBsAg WB test.

Glossary of symbols / Glossaire des symboles / Glosario de símbolos / Glossário de símbolos