WHO Prequalification of In Vitro Diagnostics
PUBLIC REPORT

Product: Bioline HCV\(^1\)
WHO reference number: PQDx 0257-012-00

Bioline HCV with product codes 02FK10, 02FK16 and 02FK17 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 29 November 2016.

### Summary of WHO prequalification assessment for Bioline HCV

<table>
<thead>
<tr>
<th></th>
<th>Date</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prequalification listing</td>
<td>29-Nov-2016</td>
<td>listed</td>
</tr>
<tr>
<td>Dossier review</td>
<td>18-Oct-2016</td>
<td>MR</td>
</tr>
<tr>
<td>Site inspection(s) of quality management system</td>
<td>28-Apr-2018</td>
<td>MR</td>
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<td>Product performance evaluation</td>
<td>8-Aug-2016</td>
<td>MR</td>
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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.

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\(^1\) Product name was changed from SD BIOLINE HCV to Bioline HCV.

\(^2\) Manufacturer’s name changed from Standard Diagnostics Inc to Abbott Diagnostics Korea Inc
<table>
<thead>
<tr>
<th>Version</th>
<th>Summary of amendment</th>
<th>Date of report amendment</th>
</tr>
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<tbody>
<tr>
<td>1.0 to 4.0</td>
<td>Inclusion of Instructions for Use.</td>
<td>8-Mar-2016</td>
</tr>
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<td>5.0</td>
<td>Correction of a typographical error</td>
<td>20-Dec-2016</td>
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<td>6.0</td>
<td>Addition of specimen collected from finger prick and subsequently two additional product codes <em>(02FK16 and 02FK17)</em></td>
<td>26-Mar-2018</td>
</tr>
<tr>
<td>7.0</td>
<td>Addition of supplier for safety lancet</td>
<td>10-Sep-2018</td>
</tr>
<tr>
<td>8.0</td>
<td>Product name was changed from SD BIOLINE HCV to Bioline HCV. Manufacturer’s name changed from Standard Diagnostics Inc to Abbott Diagnostics Korea Inc</td>
<td>3-Mar-2020</td>
</tr>
</tbody>
</table>

**Intended use:**
According to the claim of intended use from Abbott Diagnostics Korea Inc, “*the BiolineHCV is an in vitro immunochromatographic, rapid assay designed for the qualitative detection of antibodies specific to HCV, in human serum, plasma (heparin, EDTA and sodium citrate) or whole blood. Bioline HCV is intended only for professional use as the initial test, as an aid to diagnosis. Reactive specimens should be reflexed for additional testing, either by nucleic acid testing (NAT) technologies for the detection of HCV RNA or HCV core antigen testing, to identify current HCV infection. This product is intended for use in a population with high HCV prevalence or who have a history of HCV risk exposure/behaviour including pregnant women. This test may not be suitable for diagnosis of early infection or blood donation screening. The performance of the assay has not been established for populations of infants or children.*”

**Principle of the test:**

According to the claim of assay description from Abbott Diagnostics Korea Inc “*the BiolineHCV test contains a nitrocellulose membrane strip, which is pre-coated with recombinant HCV capture antigen (core, NS3, NS4 and NS5) at the test line region (T). The protein A-colloid gold conjugate and the specimen moves along the membrane chromatographically to the test region. There the antigen-antibody protein A gold particle complex forms into a visible line with high degree of sensitivity and specificity. This test device has letter “T” and “C” representing “Test Line” and “Control Line” on the surface of the case. Both the test line and control line in result window are not visible before applying the specimen. The control line is a procedural control. The*
control line should always appear if the test procedure is performed properly and the reagents in the control line are working”.  

Product test kit contents:

<table>
<thead>
<tr>
<th>Component</th>
<th>02FK10</th>
<th>02FK16</th>
<th>02FK17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specimen procedure(s)</td>
<td>Serum, plasma and whole blood (Venous whole blood and finger-prick blood)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test devices with desiccant, in individual foil pouch</td>
<td>30 T/kit</td>
<td>25 T/kit</td>
<td>25 T/kit</td>
</tr>
<tr>
<td>Assay diluent</td>
<td>1 x 5ml/vial</td>
<td>1 x 5ml/vial</td>
<td>1 x 5ml/vial</td>
</tr>
<tr>
<td>Capillary pipette(s)</td>
<td>n/a</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(10 µL each)</td>
<td>(10 µL each)</td>
</tr>
<tr>
<td>Sterile lancet(s)</td>
<td>n/a</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Sterile lancet)</td>
<td>(Safety lancet)</td>
</tr>
<tr>
<td>Alcohol swap(s)</td>
<td>n/a</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Instructions for use</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Items required but not provided:

Micropipette
Protective gloves
Timer
Biohazard container

Storage:
The test kit should be stored at 1 °C to 30 °C.

Shelf-life upon manufacture:
24 months.

Warnings/ Limitations

Refer to current version of manufacturer’s instructions for use.

Furthermore, WHO’s performance evaluation observed strong reddish background when results were read after 5 minutes, this impacted readability of the result. The operators observed
presence of reddish backgrounds (particularly in the areas above the control line and below the test line) and faint vertical lines (red/pink colour) across the reading for 43.7% specimens (211 of 483) of the WHO clinical specimen panel. It was observed that the reddish background and vertical lines dissipated between 10 – 20 minutes.

Studies to validate the reading time were submitted as part of the product dossier, these studies confirmed the claimed reading time of 5 to 20 minutes.

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

Product dossier assessment

Standard Diagnostics, Inc., submitted a product dossier for Bioline HCV 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 assessment findings were accepted on 18 October 2016.

Commitments for prequalification:
1. Validation of reading time at 30 °C and in humid conditions.
2. Real-time stability for shelf life to verify the use at 30 °C and in humid conditions.
3. Revised test device labelling including removal of dual reading legend.
4. Revised procedure for translation of labelling.

WHO followed-up on implementation of these commitments and the requirements were accepted on the 23 November 2018.

Based on the product dossier assessment findings, the product dossier for Bioline HCV meets WHO prequalification requirements.
Manufacturing site inspection

A re-inspection was performed at the site of manufacture:

- Production: Standard Diagnostics Inc., 65, Borahagal-ro, Giheung-gu, Yongin-si, Gyeonggi-do 17099 Republic of Korea and 46, Hagal-ro 15 beon-gil, Giheung-gu, Yongin-si, Gyeonggi-do 17099 Republic of Korea between 27 and 28th April 2018 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. It was confirmed that Bioline HCV was manufactured under the provisions, and in conformity with the requirements of a compliant, established QMS.

The manufacturer’s responses to the nonconformities found at the time of the inspection were accepted on 10 October 2018.

Based on the site inspection and corrective action plan review, the quality management system for Bioline HCV meets WHO prequalification requirements.

Product performance evaluation

Bioline HCV was evaluated by WHO in the second quarter of 2016 using plasma specimens. From this evaluation, we drew the following conclusions:

- Bioline HCV assay is an immunochromatographic assay for the detection of antibodies to HCV in human serum, plasma and venous whole blood.
- A volume of 10µl of specimen is needed to perform the assay.
- This type of assay does require laboratory equipment (i.e. precision pipette and tips) and can be performed in laboratories with limited facilities.

In this limited performance evaluation on a panel of 483 specimens, we found the performance summarized below:
### Performance characteristics in comparison with an agreed reference standard

<table>
<thead>
<tr>
<th></th>
<th>Initial (95% CI)</th>
<th>Final (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity %</td>
<td>98.8% (95.6 – 99.7%)</td>
<td>100% (97.76 – 100%)</td>
</tr>
<tr>
<td>Specificity %</td>
<td>100% (98.85 – 100%)</td>
<td>100% (98.85 – 100%)</td>
</tr>
<tr>
<td>Invalid rate %</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>

### Additional performance characteristics

- **Sensitivity during seroconversion on 4 seroconversion panels in comparison with a benchmark assay; DiaSorin Anti-HCV Murex EIA (Version 4.0)**: Seroconversion sensitivity index of +2.0, therefore detection is 2 days later than the benchmark assay
- **Analytical sensitivity on a mixed titer panel in comparison with an agreed reference standard**: 15 of 15 specimens were correctly classified
- **Lot to lot variation on a dilution panel in comparison with an agreed reference standard**: Acceptable

### Key operational characteristics

- **Validated specimen types**: Serum, plasma (heparin, EDTA and sodium citrate), venous whole blood
- **Number of steps**: 3 without precision required
- **Time to result**: 5 minutes
- **Endpoint stability**: 20 minutes
- **Internal QC**: Yes, the control line on the test device is an internal procedure control. Absence of the control line indicates that insufficient or improper assay diluent was added to the device.
- **In-use stability of reagents**: Until expiry date
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 02FK10

1.2 Package box for 02FK16

1.3 Package box for 02FK17
1.4 Device pouch for 02FK10, 02FK16, 02FK17
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.
5. As the test begins to work, you will see purple color move across the result window in the center of the test device.

**Test principle**

reactive specimen control.

6. Decontaminate and dispose of all specimens, reaction kits and potentially contaminated materials in a biohazard container for disposal.

- **Dispense 10 µl of drawn whole blood specimen into the specimen well marked “S”.**
- **Amber blood tubes** containing sodium citrate should be used. Other anticoagulants are not recommended.

**Application**

- **200/200 specimens of pregnant women** (including 20 specimens of multipara) were non-reactive on the Bioline™ HCV seroconversion panels.
- **3 1 1 0**

**Specificity (95 % CI)**

The diagnostic specificity calculated on 1,500 negative specimens was 100 %.

- In total 1,000 plasma specimens and 500 whole blood specimens from blood donors negative for anti-HCV with first bleeds are non-reactive with all the competitor tests, these initial faint reactions with Bioline™ HCV were considered as nonspecific and therefore this panel was not taken into account for the evaluation.
- **85 158 243**

**Interpretation of the test**

- **Resultado no reactivo:**
  - **Negativo**
  - **Reactive**

**Performance characteristics**

- **ESPAÑOL**
  - **Spanish**
  - **Português**
### Table 4. Serum/plasma equivalence (EDTA/heparin/sodium citrate)

<table>
<thead>
<tr>
<th>Test</th>
<th>Serum</th>
<th>EDTA Plasma</th>
<th>Heparin Plasma</th>
<th>Sodium Citrate Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of negative specimens</strong></td>
<td>25/25</td>
<td>25/25</td>
<td>25/25</td>
<td>25/25</td>
</tr>
</tbody>
</table>

Approx. 11.0 in Abbott Architect and S/CO approx. 3.0 in Ortho HCV version 3.0 ELISA anti HCV assays. Bioline™ HCV may exhibit prozone effect (false non-reactive result) in specimens which have higher than S/CO of results obtained on the fresh specimens and the same specimen stored for 1 to 4 days at 4 °C.

### Table 5. Result obtained in fresh enriched samples

<table>
<thead>
<tr>
<th>Test procedure</th>
<th>Procedure de la prueba</th>
<th>Procedimento do teste</th>
<th>Test interpretation</th>
<th>Interpretação do teste</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood (by venipuncture)</td>
<td>Plasma or Serum specimen</td>
<td>Echantillon de sang (par ponction veineuse), de plasma ou de sérum</td>
<td>Muestra de sangre (por venoclisis), plasma o suero</td>
<td>Amostra de sangue (por venoclise), plasma ou suero</td>
</tr>
<tr>
<td><strong>INTERPRETATION OF THE TEST / INTERPRETAÇÃO DO TESTE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NON-REACTIVE / NON RÉACTIF / NO REACTIVO / NÃO-REATIVO</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>VALID / VRAI / VÁLIDO / VÁLIDA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The presence of only the control line (C) within the result window indicates a non-reactive result.

Caution: The presence of any test line, even if very faint, the result is considered reactive.