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

	Date	Outcome
Prequalification listing	29-Nov-2016	listed
Dossier review	18-Oct-2016	MR
Site inspection(s) of quality management system	28-Apr-2018	MR
Product performance evaluation	8-Aug-2016	MR

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.

[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

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

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:

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

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		
	Initial (95% CI)	**Final (95% CI)**
Sensitivity %	98.8% (95.6 – 99.7%)	100% (97.76 – 100%)
Specificity %	100% (98.85 – 100%)	100% (98.85 – 100%)
Invalid rate %	0%	

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

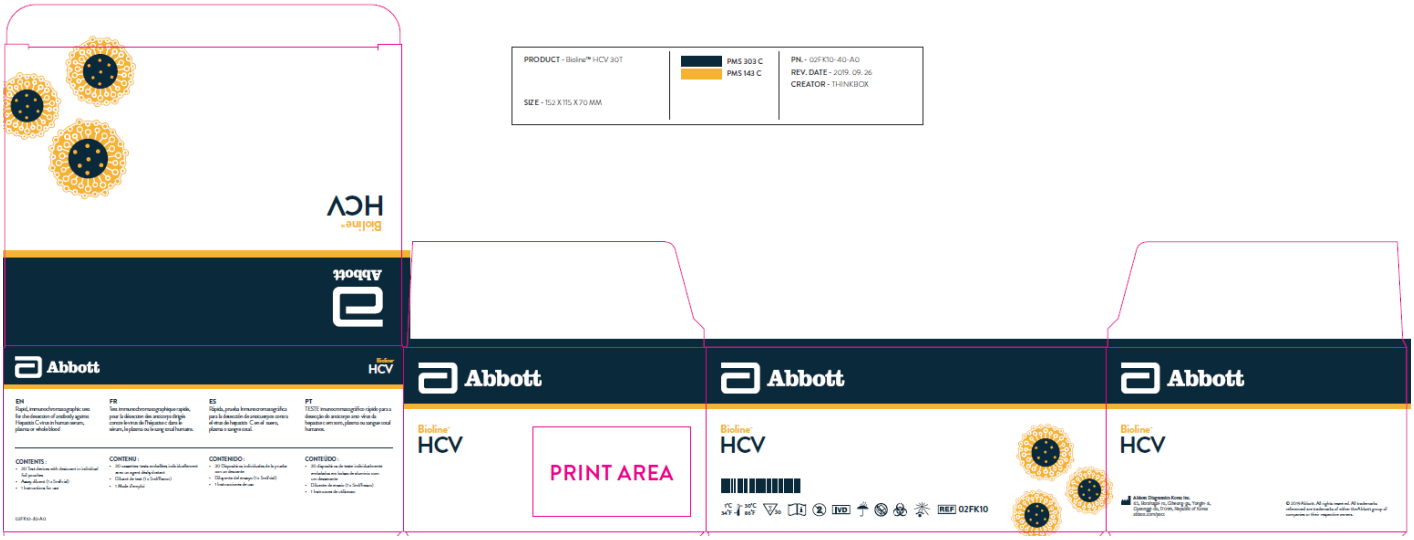
Labelling

1. **Labels**
2. **Instructions for use**

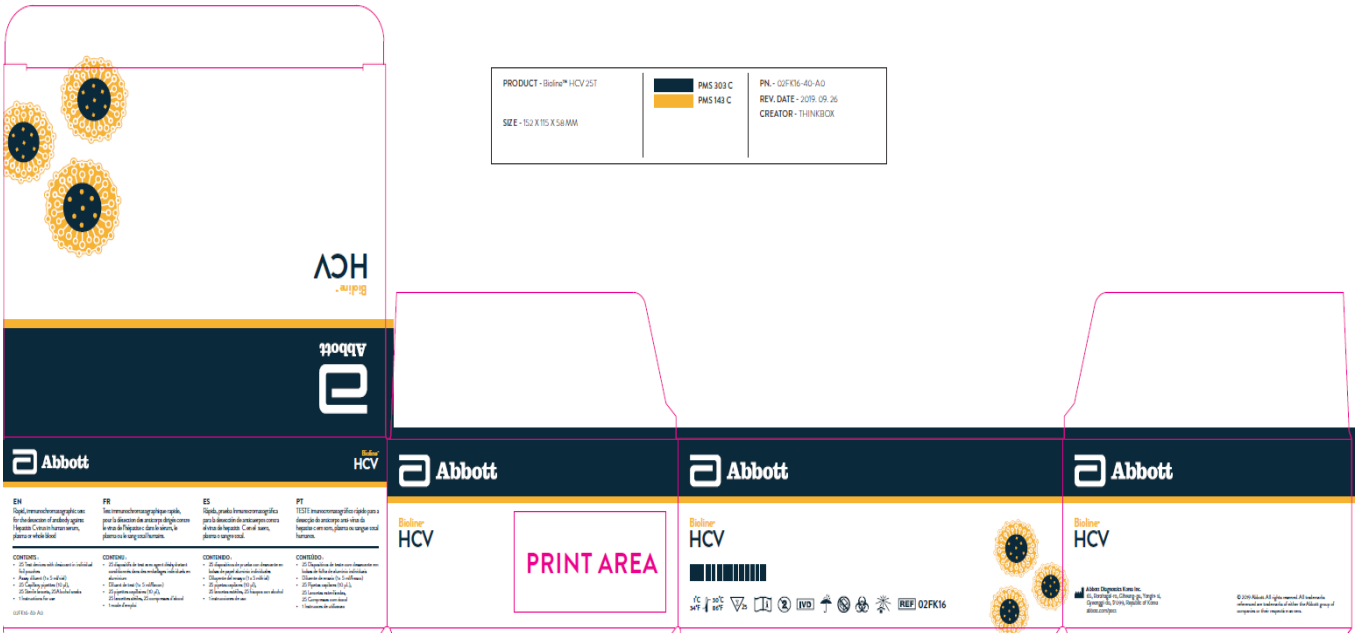
**Note: Labelling has been changed as per site name change and product rebranding. But temporarily labelling of legacy brand (SD BIOLINE) will be used in the market according to registration status in each country.*

1. Labels

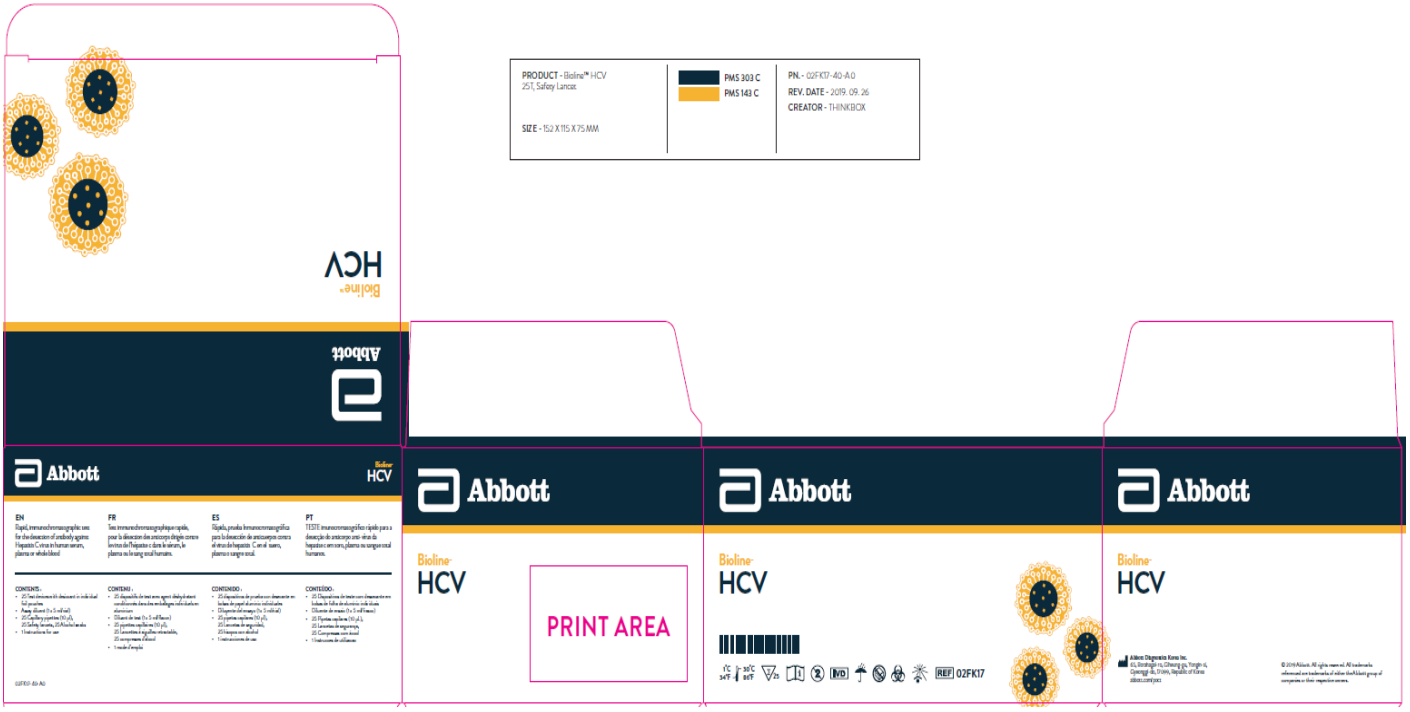
1.1 Package box for 02FK10



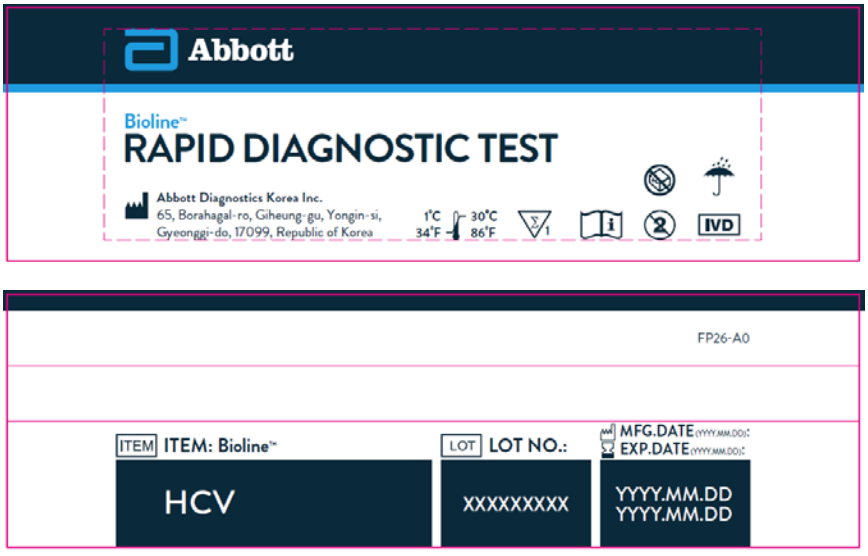
1.2 Package box for 02FK16



1.3 Package box for 02FK17



1.4 Device pouch for 02FK10, 02FK16, 02FK17



2. Instructions for use[3]

[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.

REF 02FK10/02FK16/02FK17

Abbott

Bioline™ HCV

Anti-HCV Test
Test de détection des anticorps anti-VHC
Prueba de VHC
Teste anti-VHC

ENGLISH

About the test

[Introduction] Hepatitis C virus (HCV) is recognized as a major agent of chronic hepatitis, transfusion acquired non-A, non-B hepatitis and liver disease throughout the world. HCV is an enveloped positive-sense, single-stranded RNA virus. Testing for HCV infection begins serology testing with either a rapid or a laboratory-conducted assay for HCV antibody in blood. A reactive result indicates presumptive HCV infection. When to confirm the current HCV infection it is recommended nucleic acid testing (NAT) for the detection of HCV RNA be performed following HCV antibody reactive test result. Abbott Diagnostics Korea has constructed HCV genes for the expression of recombinant antigens in bacterium systems such as *E. coli* focused on structural and non-structural immunogenic regions of the HCV-encoded polyprotein. The major immunoreactive antigens of these proteins have been reported as core, NS3, NS4 and NS5 regions of HCV genome, which are known to be highly immunodominant. For detection of HCV infection, these recombinant proteins were used as capture materials in this immunochromatographic test. Improving on the first generation HCV serologic antibody test using a single recombinant antigen, recombinant proteins with multiple antigens have been used to minimize non-specific cross-reactivity and to increase the sensitivity in this assay.

[Test principle] The Bioline™ HCV 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.

[Intended use] Bioline™ HCV 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.

Materials provided and active ingredients of main components

1. The Bioline™ HCV test kit contains the following items to perform the assay:

Catalog No.	Contents
02FK10	1. 30 Test devices with desiccant in individual foil pouches 2. Assay diluent (1 x 5 ml/vial) 3. 1 Instructions for use
02FK16	1. 25 Test devices with desiccant in individual foil pouches 2. Assay diluent (1 x 5 ml/vial) 3. 25 Capillary pipettes (10 µl), 25 Sterile lancets, 25 Alcohol swabs 4. 1 Instructions for use
02FK17	1. 25 Test devices with desiccant in individual foil pouches 2. Assay diluent (1 x 5 ml/vial) 3. 25 Capillary pipettes (10 µl), 25 Safety lancets, 25 Alcohol swabs 4. 1 Instructions for use

2. Active ingredients of main components
- 1 Test device includes:
  - Gold conjugates: Protein A – gold colloid (1.0±0.2 µg)
  - Test line: Recombinant HCV antigen (core, NS3, NS4, NS5) (1.5±0.3 µg)
  - Control line: Goat anti-human Immunoglobulin (2.0±0.4 µg)
- Assay diluent includes: 50 mM Tris-HCl Buffer (5 ml), Sodium azide (0.02 %)

Materials required but not provided

- Micropipette, Protective gloves, Timer, Biohazard container

Kit storage and stability

1. The test kit should be stored at a temperature between 1 °C and 30 °C. Do not freeze the kit or its components.
2. Assay diluent may be opened and resealed for each assay. Cap should be firmly sealed between each use. Assay diluent is stable until expiration date if kept at 1 - 30 °C.
3. The test device is sensitive to both heat and humidity. Perform the test immediately after removing the test device from foil pouch.
4. Do not use the test kit beyond its expiration date. The shelf life of the kit is as indicated on the outer package.
5. Do not use the test kit if the pouch is damaged or the seal is broken.

Warnings

1. The test devices are for *in vitro* diagnostic use only. Do not reuse the test device.
2. The instructions must be followed exactly to achieve accurate results. Any individual performing an assay with this product must be trained in its use and must be proficient.
3. Do not use the pipette by mouth, smoke, drink, eat, apply cosmetics, or handle contact lenses in areas where specimens or kit components are being handled.
4. Wear protective gloves while handling specimens and wash hands thoroughly afterwards.
5. Clean up spills thoroughly using an appropriate disinfectant.
6. Decontaminate and dispose of all specimens, reaction kits and potentially contaminated materials in a biohazard container as if they were infectious waste.
7. Do not mix or interchange different specimens.
8. Do not eat the desiccant from the foil pouch.
9. Avoid splashing or aerosol formation of specimen and assay diluent.
10. Do not mix or interchange components among different lots or those for other products.
11. Do not drink assay diluent.
12. Care should be taken to avoid contamination of the bottle nozzle when dropping assay diluent into the specimen well.
13. The assay diluent contains a proprietary anti-microbial agent, sodium azide, which presents no hazard to the user if normal laboratory safety precautions are followed. If contact with assay diluent to the eyes and/or skin, wash affected area with soap and water immediately. If irritation or signs of toxicity occur, seek medical attention.
14. The assay diluent contains sodium azide, which may react with lead or copper plumbing to form highly explosive metal azide compounds. When disposing of these reagents through plumbing fixtures, flush with a large volume of water to prevent azide build-up in drains.
15. Even though the color of assay diluent is changed to faint yellow, it doesn't affect the performance and stability of the kit.

Specimen collection and storage

1. Whole blood

[Collection by venipuncture]
- Using venipuncture, draw whole blood into the collection tube (containing anticoagulants including heparin, EDTA and sodium citrate).
- If the blood specimen is not immediately tested, it must be refrigerated at 2 - 8 °C.
- If stored at 2 - 8 °C, the blood specimen must be tested within 3 days of refrigeration.
- Do not use a blood specimen stored for more than 3 days; it can cause a nonspecific reaction.
- Bring blood specimens to room temperature (15 - 30 °C) prior to use.

[Collection using a lancet]
- Clean the area to be lanced with an alcohol swab.
- Squeeze the fingertip then prick the lateral side of the finger with a lancet provided. Wipe away the first blood drop. Then, safely dispose of the lancet immediately after.
- Immerse the open end of a new capillary pipette (10 µl) in the next blood drop and release the pressure to draw blood into the capillary pipette up to the fill line.

2. Plasma or serum
- [Plasma] Using venipuncture, draw the whole blood into the collection tube (containing anticoagulants including heparin, EDTA and sodium citrate) and then centrifuge blood to obtain the plasma specimen.
- [Serum] Using venipuncture, draw the whole blood into the collection tube (NOT containing anticoagulants) then leave for 30 minutes to allow blood coagulation to occur. Centrifuge the tube to generate a serum specimen.
- If plasma or serum specimens are not tested immediately, they must be refrigerated at 2 - 8 °C. For storage period longer than 2 weeks, freezing (below -20 °C) is required. Bring plasma or serum specimens to room temperature (15 - 30 °C) prior to use.
- Plasma or serum specimens containing a precipitate may yield inconsistent test results. Such specimens must be clarified by centrifugation prior to assaying.

3. Precautions
- Repeated frozen-thawed cycle for specimen should be avoided.
- Anticoagulants including heparin, EDTA and sodium citrate do not affect the test result. Use of other anticoagulants has not been validated. Their use may affect the test result.
- Use new pipette tips for each specimen in order to avoid cross-contamination of other specimens which could cause erroneous results.

Test procedure

1. Bring all kit components and specimens to reach a temperature between 15 °C and 30 °C prior to testing.
2. Remove the test device from foil pouch and place it on a flat, dry surface. Label the test device with a patient identifier.
3. **[Using a micropipette]**
   Dispense 10 µl of plasma, serum or whole blood specimen into the specimen well marked "S".
   Or,
   [Using a capillary pipette]
   Dispense 10 µl of drawn whole blood specimen into the specimen well marked "S".
4. Dispense 4 drops of assay diluent into the specimen well "S".
   ⚠ **Caution:** If you do not hold the bottle vertically, it can lead to inaccurate results. Exactly, 4 drops should be added. Adding more than 4 drops may result in reddish color background or an invalid result.
5. As the test begins to work, you will see purple color move across the result window in the center of the test device.
6. Interpret test results 5 - 20 minutes after adding assay diluent. Do not read after 20 minutes.
   ⚠ **Caution:** If the test result is not legible after 5 minutes due to high background color, read again later but within 20 minutes of adding the diluent. Reading outside of this time frame (before 5 min or after 20 min) may result in false results.

Test interpretation

1. A colored control line will appear at "C" in the result window to show that the test is working properly.
2. The "T" section of the result window indicates the test result.
- **Non-reactive result:** The presence of only the control line (C) within the result window indicates a non-reactive result.
- **Reactive result:** The presence of the test line (T) and the control line (C) within the result window, regardless of which line appears first, indicates a reactive result.
  ⚠ **Caution:** The presence of any test line, no matter how faint, the result is considered reactive.
- **Invalid result:** If the control line (C) is not visible within the result window after performing the test, the result is considered invalid. Instructions may not have been followed correctly or the test may have deteriorated. It is recommended that the specimen be retested using a new test device.

Test limitations

1. A non-reactive result does not preclude the possibility of infection with HCV. Other clinically available tests are required if questionable results are obtained. As with all diagnostic tests, a definitive clinical diagnosis should not be based on the result of a single test, but should only be made by the physician after all clinical and laboratory findings have been evaluated.
2. Due to the inherent design of qualitative IVD tests, a faint or absent test line (false non-reactive) may occur in specimens containing high antibody densities; the prozone effect. In order to obtain a definitive result, all clinical and laboratory findings should be evaluated.

Internal quality control

The Bioline™ HCV test device has 2 pre-coated lines on the surface of the test: "T" (test line) and "C" (control line). Neither the test line nor the control line is visible in the result window before applying a specimen. The control line is used for procedural control and shows only that the diluent has been applied successfully and that the active ingredients of the main components on the strip are functional, but it is not an assurance that the specimen has been properly applied; it is not a reactive specimen control.

Performance characteristics

1. The Bioline™ HCV test kit is designed to have 99.3 % (95 % CI: 96.1 - 99.9 %) of sensitivity and 98.1 % (95 % CI: 94.5 - 99.4 %) of specificity.
   A total of 299 serum specimens collected from Korea were tested on the Bioline™ HCV in Korea. The serum specimens were comprised of 142 positive and 157 negative clinical serum specimens confirmed by a leading commercial anti-HCV ELISA test. The results gave sensitivity of 99.3 % (141/142), a specificity of 98.1 % (154/157).

Reference assay		Bioline™ HCV		Total Results
		Reactive	Non-reactive	
Anti-HCV ELISA	Positive	141	1	142
	Negative	3	154	157
Sensitivity (95 % CI)		99.3 % (96.1 - 99.9 %)		
Specificity (95 % CI)		98.1 % (94.5 - 99.4 %)		

Even though our intended performance is as above, the results of individual laboratories may vary from these data because the results can be unique to the population it serves depending upon geographical, patient, dietary, environmental and other factors.

2. Bioline™ HCV test kit has been evaluated in 4 different sites as below.

1) Study 1
   A total of 1,187 serum specimens collected from Korea were tested on the Bioline™ HCV in Korea. The serum specimens were comprised of 157 positive and 1,030 negative clinical serum specimens confirmed by a leading commercial anti-HCV ELISA test. The specimens repeatedly reactive both by ELISA and Bioline™ HCV were tested by the confirmatory assay using RT-PCR.

Reference assay		Bioline™ HCV		Total Results
		Reactive	Non-reactive	
Anti-HCV ELISA	Positive	157	0	157
	Negative	6	1,024	1,030
Sensitivity (95 % CI)		100 % (97.6 - 100 %)		
Specificity (95 % CI)		99.4 % (98.7 - 99.7 %)		

2) Study 2 : European performance evaluation according to the common technical specification (2009/886/EC)

2-1) Diagnostic sensitivity for anti-HCV detection
- Anti-HCV positive specimens
  410 anti-HCV positive specimens were tested by Sanquin in the Netherlands and the German Red Cross. The diagnostic sensitivity for anti-HCV antibody detection, calculated on 410 positive specimens, was 99.3 %.

  Table 1. Result obtained with the Bioline™ HCV on all Anti-HCV positive specimens

	Bioline™ HCV	
	Reactive	Non-reactive
Anti-HCV positive serum/plasma (n=213)	211	2
Anti-HCV positive whole blood/plasma couples (n=100)	100	0
Anti-HCV with known genotype (n=97)	96	1
Total (n=410)	407	3
Sensitivity (95 % CI)	99.3 % (97.9 - 99.8 %)	

- Anti-HCV positive serum/plasma
  213 anti-HCV positive specimens confirmed with CHIRON HCV RIBA™ 3.0 SIA or INNO-LIA HCV Score without genotype information were tested at Sanquin. In two specimens the Bioline™ HCV obtained a non-reactive result.
- Anti-HCV positive whole blood/plasma couples (Paired specimens)
  100 paired whole blood and plasma specimens anti-HCV positive with Abbott Architect anti-HCV, taken from HCV infected patients were tested at the German Red Cross. The Bioline™ HCV test was reactive on all 100 paired specimens.
- Anti-HCV with known genotype
  94 specimens from patients with a known HCV genotype 1 to 6, based on the VERSANT HCV Genotype 2.0 Assay (LiPA) were tested by Sanquin, and 3 specimens of genotype 5 were tested by the German Red Cross.

  Table 2. Anti-HCV positive specimens with known genotype

HCV genotype		# Specimens	Bioline™ HCV Reactive	Bioline™ HCV Non-reactive
Genotype 1 (n=23)	1	1	1	0
	1a	10	10	0
	1b	12	11	1*
Genotype 2 (n=22)	2a/2c	13	13	0
	2b	9	9	0
Genotype 3 (n=25)	3	1	1	0
	3a	22	22	0
	3b	1	1	0
	3k	1	1	0
Genotype 4 (including non 4a) (n=20)	4a/4c/4d	4	4	0
	4c/4d	14	14	0
	4h	2	2	0
Genotype 5 (n=5)	5a	2	2	0
	5	3	3	0
Genotype 6 (n=2)	6	1	1	0
	6a	1	1	0

*One genotype 1b specimen was non-reactive on the Bioline™ HCV.

- Sensitivity on seroconversion panels
  20 commercially available seroconversion panels (SeraCare Life Sciences and Zeptometrix) were tested with Bioline™ HCV by Sanquin.
  In total 54 specimens were tested reactive with Bioline™ HCV and 47 with the competitor tests.

Panel ID	Bioline™ HCV	Ortho HCV 3.0 or Ortho Enhanced SAVe Anti-HCV 3.0 (*)
PHV904	3/7	3/7
PHV905	3/9	4/9
PHV911	3/5	3/5
PHV913	0/4	0/4
PHV914	5/9	3/9
PHV915	2/4	2/4
PHV918	1/8	2/8
PHV919 (a)	7/7	3/7
PHV920	6/10	6/10
6213	2/12	2/12
6214	6/13	4/13
6224	2/6	0/6
6226	4/12	3/12
6228	3/12	3/12
6229	3/8	3/8
9044	2/6	2/6
9045	2/8	1/8
9047	4/10	4/10
9054	1/10	1/10 (*)
9058	2/5	1/5 (*)
Total reactive bleeds (a)	54	47

(a): The Bioline™ HCV test obtained faint reactive lines on all panel members of panel PHV919. Since the 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.

2-2) Diagnostic specificity
   In total 1,000 plasma specimens and 500 whole blood specimens from blood donors negative for anti-HCV with ABBOTT PRISM were tested. The specimens originated from 2 collection sites in Germany, Frankfurt and Ulm. The diagnostic specificity calculated on 1,500 negative specimens was 100 %.

   Table 3. Diagnostic specificity on anti-HCV negative blood donors

	Bioline™ HCV	
	Reactive	Non-reactive
Blood donors plasma specimens	0	1,000
Blood donors whole blood specimens	0	500
Specificity (95 % CI)	100% (99.7 - 100 %)	

3) Study 3 : WHO laboratory evaluation
- WHO HCV specimen reference panels
  The 483 specimens that clinically derived serum/plasma specimens from Australian, European, African, Latin American and Asian origin was tested on the Bioline™ HCV. There were 163 anti-HCV positive specimens and 320 anti-HCV negative specimens. Each specimen was confirmed by commercial EIA tests, Murex anti-HCV EIA version 4.0 (DiaSorin S.A. Italy) and Monolisa anti-HCV PLUS version 2.0 (Biorad Laboratories).

Reference assay		Bioline™ HCV		Total Results
		Reactive	Non-reactive	
EIA	Positive	163	0	163
	Negative	0	320	320
Sensitivity (95 % CI)		100 % (97.8 - 100 %)		
Specificity (95 % CI)		100 % (98.8 - 100 %)		

- HCV seroconversion panels
  In four different seroconversion panels (PHV913, PHV919, PHV920 and PHV922), the Bioline™ HCV detected antibodies to HCV on average 3 specimens later than the reference assay (DiaSorin Anti-HCV Murex EIA, Version 4.0).
- HCV performance panels
  The Bioline™ HCV assay detected 15/15 HCV antibody positive specimens in the HCV mix titre performance panel (0810-0175) and 8/10 HCV antibody positive specimens in the HCV low titre performance panel (0810-0192).

4) Study 4
   Specimens were collected from 243 persons in Bangladesh with four (4) types of blood (serum, plasma, venous whole blood, and finger prick blood). Bioline™ HCV kit showed 100% (243/243) equivalent result to the 3 types of specimen corresponding serum, plasma, and venous whole blood. In case of finger prick blood, there was only one discordance specimen, it was given 99.6% (242/243) agreement with other specimen types. This specimen was confirmed as weak positive by a commercial anti-HCV assay.

Specimen type		Finger prick blood		
		Positive	Negative	Total
Serum, plasma, venous whole blood	Positive	85	1*	86
	Negative	0	157	157
	Total	85	158	243
Agreement (95 % CI)		99.6 % (97.7 - 99.9 %)		

*The specimen was weak positive of Hepatitis C confirmed by commercial anti-HCV assay.

3. Analytical performance

1) Analytical specificity
- 200/200 hospitalized patients were non-reactive on the Bioline™ HCV.
- 200/200 specimens of pregnant women (incl. 20 specimens of multipara) were non-reactive on the Bioline™ HCV.
- 100/100 specimens containing potentially cross reactive substances were non-reactive on the Bioline™ HCV (20 Anti-HBs positive, 20 Anti-HBc positive, 20 Anti-HIV positive, 10 Anti-HTLV I/II positive, 20 Anti-HEV positive, 10 Rheumatoid factor positive).
- The following potential cross-reacting pathogens had no effect on test results of Bioline™ HCV.

Anti-HBs	CMV	HIV	Syphilis
Borrelia burgdorferi	EBV	HTLV	Toxoplasma
Chlamydia	HBsAg	Influenza	*Trypanosoma cruzi* I / II

- The following 9 potential interfering substances had no effect on test results of Bioline™ HCV; Pregnant women, high cholesterol (≥240 mg/dL), high bilirubin (≥1.4 mg/dL), Rheumatoid factor (≥28.2 IU/ml), lipemic, hemolyzed, autoimmune, alcoholic cirrhosis, multiparous pregnancy
- Pharmaceutical substances
  There was no significant interference with the following 25 drugs on Bioline™ HCV. All drugs were tested at concentrations of 250 µg/mL.

Abacavir	Ergocalciferol	Naproxen
Acetaminophen	Folic acid	Nevirapine
Acetylsalicylic acid	Hydrochlorothiazide	Pantoprazole
Amoxicillin	Ibuprofen	Pyrazinamide
Aspirin	Iron Chloride	Rifampicin
Cholecalciferol	Isoniazid	Ritonavir
Cyclobenzaprine	L-ascorbic acid	Salicylic acid
Darunavir	Magnesium sulfate	
Diclofenac	Metformin	

2) Prozone effect
Bioline™ HCV may exhibit prozone effect (false non-reactive result) in specimens which have higher than 5ICO of approx. 11.0 in Abbott Architect and SiCO approx. 3.0 in Ortho HCV version 3.0 ELISA anti HCV assays.

3) Specimen matrix
Validation on whole blood was done by testing 500 negative and 100 positive anti-HCV specimens. The performance of Bioline™ HCV on whole blood was comparable to the performance on plasma specimens. (See table 1 and table 3 presented in study 2 above.) Validation on serum and different plasma specimen types (EDTA / Heparin / Sodium citrate) was performed by German Red Cross. The results obtained on negative and positive specimens are identical in serum, EDTA plasma, heparin plasma and citrate plasma.

Table 4. Serum/plasma (EDTA / Heparin / Sodium citrate) equivalence

Specimen type	No. of Bioline™ HCV reactive/No. of positive specimens	No. of Bioline™ HCV non-reactive/ No. of negative specimens
Serum	25/25	25/25
EDTA plasma	25/25	25/25
Heparin plasma	25/25	25/25
Na-Citrate plasma	25/25	25/25

4) Complement factors interference in fresh serum specimens
In total 25 negative specimens, spiked with an anti-HCV positive specimen were tested within 24 hours after collection and retested after being stored at 4 °C for 1, 2, 3 and 4 days. No differences were observed on the results obtained on the fresh specimens and the same specimen stored for 1to 4 days at 4 °C.

Table 5. Result obtained on spiked fresh specimens

		Bioline™ HCV	
		Reactive	Non-reactive
25 negative specimens	**day 0**	0	25
	day 0	25	0
25 negative specimens spiked with anti-HCV	**day 1**	25	0
	day 2	25	0
	day 3	25	0
	day 4	25	0

5) Reproducibility of the Bioline™ HCV has been demonstrated by within-run, between-run, and batch-to-batch studies using in-house reference panels. All values were identical to reference panel acceptance criteria.

Product Disclomer:
While every precaution has been taken to ensure the diagnostic ability and accuracy of this product, the product is used outside of the control of the manufacturer and distributor and test results may accordingly be affected by environmental factors and/or user error. The subject of the diagnosis should consult a doctor for further confirmation of the test result.

Warning:
The manufacturers and distributors of this product shall not be liable for any direct, indirect, or consequential losses, liability, claims, costs or damages arising from or related to an incorrect reactive or non-reactive result using this product.

3) Matrice d'échantillons
La validation sur sang total a été réalisée en testant 500 échantillons négatifs pour les anticorps anti-VHC et 100 échantillons positifs. Les performances du test Bioline™ HCV sur sang total étaient comparables à ses performances sur des échantillons de plasma (voir les tableaux 1 et 3 présentés pour l'étude 2 ci-dessus). La validation sur sérum et sur différents types d'échantillon de plasma (EDTA/héparine/citrate de sodium) a été réalisée par la Croix Rouge allemande. Les résultats obtenus pour les échantillons positifs et négatifs sont identiques pour le sérum, la plasma avec EDTA, le plasma avec héparine et le plasma avec citrate.

Tableau 4. Équivalence sérum/plasma (EDTA/héparine/citrate de sodium)

Type d'échantillon	Nbre d'échantillons Bioline™ HCV réactifs/ nbre d'échantillons positifs	Nbre d'échantillons Bioline™ HCV non réactifs/nbre d'échantillons négatifs
Sérum	25/25	25/25
Plasma EDTA	25/25	25/25
Plasma héparine	25/25	25/25
Plasma Na-citrate	25/25	25/25

4) Interférence des facteurs du complément dans les échantillons de sérum frais
Au total, 25 échantillons négatifs additionnés d'un échantillon positif pour les anticorps anti-VHC ont été testés dans les 24 heures suivant leur prélèvement, puis de nouveau après conservation à 4 °C pendant 1, 2, 3 et 4 jours. Aucune différence n'a été observée entre les résultats obtenus avec les échantillons frais et les mêmes échantillons conservés pendant 1à 4 jours à 4 °C.

Tableau 5. Résultats obtenus sur les échantillons frais additionnés d'échantillon positif

		Bioline™ HCV	
		Réactif	Non réactif
25 échantillons négatifs	**jour 0**	0	25
	jour 0	25	0
25 échantillons négatifs additionnés d'anticorps anti-VHC	**jour 1**	25	0
	jour 2	25	0
	jour 3	25	0
	jour 4	25	0

5) La reproductibilité du test Bioline™ HCV a été démontrée par des études inter-cycles et intra-cycles et inter-lots, à l'aide de groupes de référence internes. Toutes les valeurs étaient identiques aux critères d'acceptation des panels de référence.

Clause de non-responsabilité :
Bien que toutes les précautions aient été prises pour garantir les performances diagnostiques et la précision de ce produit, il est utilisé en dehors du contrôle du fabricant et du distributeur. Les résultats peuvent donc être influencés par des facteurs environnementaux et/ou une erreur d'utilisation. Il est fortement recommandé au patient ayant reçu le diagnostic de consulter un médecin pour confirmer le résultat du test.

Avertissement :
Les fabricants et les distributeurs de ce produit ne peuvent, en aucune manière, être tenus responsables des pertes, dommages, réclamations ou coûts, quels qu'ils soient, directs, indirects ou consécutifs, dus ou liés à un diagnostic réactif ou non réactif erroné établi à l'aide de ce produit.

4) Interferencia de factores complementarios en muestras de suero fresco
En total, se evaluaron 25 muestras negativas, enriquecidas con una muestra positiva de anti-VHHC, dentro de las 24 horas siguientes a la extracción y se volvieron a evaluar después de estar almacenadas a 4 °C durante 1, 2, 3 y 4 días. No se observaron diferencias en los resultados obtenidos en las muestras frescas y en las mismas muestras almacenadas por 1 a 4 días a 4 °C.

Tabla 5. Resultado obtenido en muestras frescas enriquecidas

		Bioline™ HCV	
		Reactivo	No reactivo
25 muestras negativas	**día 0**	0	25
25 muestras negativas enriquecidas con anti-VHC	**día 0**	25	0
	día 1	25	0
	día 2	25	0
	día 3	25	0
	día 4	25	0

5) Se demostró la reproducibilidad de la prueba Bioline™ HCV con estudios dentro de una misma serie, entre series y entre diferentes lotes, con paneles de referencia internos. Todos los valores obtenidos fueron idénticos a los criterios de aceptabilidad del panel de referencia.

Advertencia sobre el producto:
Se han tomado todas las precauciones para garantizar la capacidad y la precisión diagnóstica de este producto. No obstante, el producto se usa fuera del control del fabricante o distribuidor y, de esa manera, los resultados pueden verse afectados por factores ambientales o error del usuario. El sujeto del diagnóstico debe consultar a un profesional para confirmar el resultado de la prueba.

Advertencia:
Los fabricantes y distribuidores de este producto no serán responsables por pérdidas directas, indirectas o derivadas, obligaciones, reclamos, costos o daños vinculados o relacionados con un resultado reactivo o no reactivo incorrecto utilizando este producto.

4) Interferência de fatores complementares e amostras de soro frescas
No total, 25 amostras fortificadas com uma amostra de anti-VHC positiva foram testadas no espaço de 24 horas após colheita e novamente testadas após estarem armazenadas a 4 °C durante 1, 2, 3 e 4 dias. Não foram observadas diferenças nos resultados obtidos nas amostras frescas e na mesma amostra armazenada durante 1 a 4 dias a 4 °C.

Quadro 5. Resultado obtido em amostras frescas fortificadas

		Bioline™ HCV	
		Reativo	Não-reativo
25 amostras negativas	**dia 0**	0	25
25 amostras negativas fortificadas com anti-VHC	**dia 0**	25	0
	dia 1	25	0
	dia 2	25	0
	dia 3	25	0
	dia 4	25	0

5) A reprodutibilidade do teste Bioline™ HCV foi demonstrada por estudos intraensaio, entre ensaios e de lote-para-lote utilizando painéis de referência internos. Todos os valores foram idênticos aos critérios de aceitação dos painéis de referência.

Renúncia de produto:
Embora tenham sido tomadas todas as precauções para garantir a capacidade e exatidão de diagnóstico deste produto, a mesma é utilizada fora do controlo do fabricante e distribuidor, pelo que os resultados dos testes poderão ser afetados em conformidade com fatores ambientais e/ou erros dos utilizadores. A pessoa a quem se aplica o diagnóstico deve consultar um médico para confirmar posteriormente o resultado.

Aviso:
Os fabricantes e os distribuidores deste produto não se responsabilizam por quaisquer perdas diretas, indiretas ou consequenciais, compensações, reclamações, custos ou danos resultantes ou relacionados com um diagnóstico incorreto, seja este reativo ou não reativo, aquando da utilização do produto.

Bibliography of suggested reading / Bibliographie

1. Ansah G., Czeslaw W., Chao Lin, Stephen M. Feinstone, and Charles M. Rice : Expression and Identification of Hepatitis C Virus Polyprotein Cleavage Products. Journal of Virology, March. 1993, p.1385-1395
2. Young Gyu Cho, Min Kyung Yi, Kyung Lib jang, Chang Min Kim and Young Chul Sung : Cloning and Overexpression of the Highly Immunogenic Region of HCV Genome from Korean Patients. Mol. Cells, Vol. 3, 4-7 : 416
3. S. Osborne, E. Cecconato, S. Grira, F. Garetto, R. Calegero, C. Rosa and F. Bonelli : Expression in *E. coli* and purification of a chimeric p22-NS3 recombinant antigen of Hepatitis C Virus(HCV). Federation of European Biochemical Societies, Volume 324, number 3, 253-257
4. A. Yoshikawa, K. Takahashi, S. Kishimoto : Serodiagnosis of hepatitis C virus infection by ELISA for antibodies against the putative core protein (p20C) expressed in Escherichia coli. Journal of Immunological Methods, 148 (1992) 143-150
5. Mitchell B.L. et al, Impact freeze-thaw cycles and storage time on plasma samples used in mass spectrometry based biomarker discovery projects. Cancer Informatics, 2005;598-104
6. Cuhadar S. et al, The effect of storage time and freeze-thaw cycles on the stability of serum samples. Biochemia Media, 2013;23(1):70-77

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PREPARATION / PRÉPARATION /PREPARACIÓN / PREPARAÇÃO

1

EN **Open the package and look for the following:**
1. Test device with desiccant in individual foil pouch
2. Assay diluent
3. Instructions for use

ES **Abra el paquete y busque los siguientes elementos:**
1. Dispositivo de prueba con desecante en bolsa de papel aluminio individual
2. Diluyente del ensayo
3. Instrucciones de uso

FR **Ouvrir l'emballage et identifier les éléments suivants :**
1. Dispositif de test avec agent déshydratant conditionné dans un emballage en aluminium individuel
2. Diluant du test
3. Mode d'emploi

PT **Abra a embalagem e procure o seguinte:**
1. Dispositivo de teste com dessecante em bolsa de folha de alumínio individual
2. Diluente de ensaio
3. Instruções de utilização

Including only for Catalog No. 02FK16 and 02FK17

Contenu, numéros catalogue 02FK16 et 02FK17 uniquement

Incluidos solo para los N.º de catálogo 02FK16 y 02FK17

Incluídas apenas para os códigos de catálogos 02FK16 e 02FK17

EN
1. Capillary pipette (10 µl)
2. Lancet
3. Alcohol swab

ES
1. Pipeta capilar (10 µl)
2. Lanceta
3. Hisopo con alcohol

FR
1. Pipette capillaire (10 µl)
2. Lancette
3. Compresse d'alcool

PT
1. Pipeta capilar (10 µL)
2. Lanceta
3. Zaragatoa com álcool

2

EN Carefully read the instructions on how to use the Bioline™ HCV test kit.

ES Lea con atención las instrucciones de uso del kit de prueba Bioline™ HCV.

FR Lire attentivement le mode d'emploi du kit de test Bioline™ HCV.

PT Leia com atenção as instruções de utilização do kit de teste Bioline™ HCV.

3

EN Look at the expiration date at the back of the foil pouch. If the expiration date has passed, use another kit. To avoid false results, ensure that the assay diluent used is from the same kit as the new test device.

ES Lea la fecha de vencimiento indicada en la parte posterior de la bolsa. Si la fecha ya ha pasado, use otro kit. Para evitar falsos resultados, asegúrese de que el diluyente del ensayo utilizado sea del mismo kit que el dispositivo de prueba nuevo.

FR Vérifier la date de péremption à l'arrière de l'emballage en aluminium. Si elle est dépassée, utiliser un autre kit. Pour éviter d'obtenir des résultats erronés, veiller à utiliser le diluant du test provenant du même kit que le nouveau dispositif de test.

PT Verifique o prazo de validade na parte posterior da bolsa de folha de alumínio. Se o prazo de validade tiver sido ultrapassado, utilize outro kit. Para evitar resultados falsos, certifique-se de que o diluente do ensaio utilizado é do mesmo kit que o novo dispositivo do teste.

4

EN **Open the foil pouch and look for the following:**
1. Test device
2. Desiccant

Then, label the device with the patient identifier.

ES **Abra la bolsa de papel aluminio y busque los siguientes elementos:**
1. Dispositivo de prueba
2. Desecante

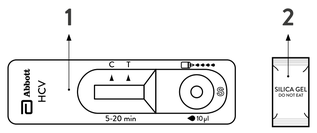
Luego, etiquete el dispositivo de prueba con un identificador del paciente.

FR **Ouvrir l'emballage en aluminium et identifier les éléments suivants :**
1. Dispositif de test
2. Agent déshydratant

Apposer ensuite une étiquette indiquant l'identifiant du patient sur le dispositif de test.

PT **Abra a bolsa de folha de alumínio e procure o seguinte:**
1. Dispositivo de teste
2. Dessecante

Em seguida, coloque uma etiqueta no dispositivo com o identificador do paciente.



10 µl : 10 µl of serum, plasma or whole blood specimen / 10 µl d'échantillon de sérum, de plasma ou de sang total / 10 µl de la muestra de suero, plasma o sangre/ 10 µl de amostra de soro, plasma ou de sangue total

: Assay diluent 4 drops / Diluant du test 4 gouttes / Diluyente del ensayo 4 gotas/ Diluente de ensaio 4 gotas

TEST PROCEDURE / PROCÉDURE DE TEST / PROCEDIMIENTO DE LA PRUEBA / PROCEDIMENTO DO TESTE

I. Blood (by venipuncture), Plasma or Serum specimen / I. Échantillon de sang (par ponction veineuse), de plasma ou de sérum / I. Muestra de sangre (por venopunción), plasma o suero / I. Amostra de sangue (por punção venosa), plasma ou soro

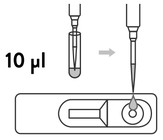
1

EN Take 10 µl of serum, plasma or whole blood specimen using a micropipette.
Dispense 10 µl of serum, plasma or whole blood specimen into the specimen well "S".

FR Prélever **10 µl d'échantillon de sérum, de plasma ou de sang total** à l'aide d'une micropipette.
Déposer 10 µl d'échantillon de sérum, de plasma ou de sang total dans le puits d'échantillon « S ».

ES Con una micropipeta, tome **10 µl de la muestra de suero, plasma o sangre.**
Instile 10 µl de la muestra de suero, plasma o sangre en el espacio para muestras "S".

PT Tire **10 µl de amostra de soro, plasma ou de sangue total** com uma micropipeta.
Deite 10 µl de amostra de soro, plasma ou sangue total no poço da amostra "S".



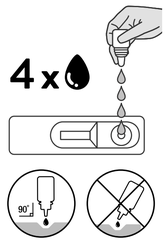
2

EN **Hold assay diluent bottle vertically and dispense 4 drops of assay diluent** into the specimen well "S". **Exactly, 4 drops should be added.** Do not let bottle tip touch device in order to avoid cross-contamination.

FR **Tenir le flacon de diluant du test à la verticale et déposer 4 gouttes dans** le puits d'échantillon « S ». **Il faut ajouter très exactement 4 gouttes.** Ne pas mettre l'embout du flacon en contact avec le dispositif afin d'éviter toute contamination croisée.

ES **Sostenga la botella del diluyente del ensayo en forma vertical y deposite 4 gotas del diluyente** del ensayo en los pocillos para muestras "S". **Agregue exactamente 4 gotas.** No permita que la punta de la botella entre en contacto con el dispositivo a fin de evitar la contaminación cruzada.

PT **Mantenha o frasco de diluente do ensaio na posição vertical e deite 4 gotas de diluente** do ensaio no poço para o poço da amostra "S". **Devem ser adicionadas, exatamente, 4 gotas.** Não deixe a ponta do frasco tocar no dispositivo de modo a evitar a contaminação cruzada.



3

EN Interpret test results 5 - 20 minutes after adding assay diluent. Reading outside of this time frame (before 5 min or after 20 min) may provide false results.

FR Interpréter les résultats du test 5 à 20 minutes après l'ajout du diluant. Toute lecture en dehors de cette période (avant 5 minutes ou après 20 minutes) peut donner lieu à des résultats erronés.

ES Una vez transcurridos de 5 a 20 minutos de haber agregado el diluyente del ensayo, interprete los resultados. Leer el resultado fuera de ese marco de tiempo (antes de los 5 minutos o después de los 20 minutos) puede arrojar resultados falsos.

PT Interprete os resultados do teste 5 - 20 minutos após adicionar o diluente do ensaio. Efetuar a leitura fora deste intervalo de tempo (antes dos 5 minutos ou após os 20 minutos) pode fornecer resultados incorretos.

II. Blood specimen (with a lancet) / II. Échantillon de sang (avec une lancette) / II. Muestra de sangre (con una lanceta) / II. Amostra de sangue (com uma lanceta)

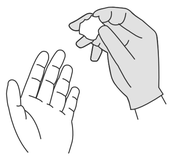
1

EN Clean the area to be lanced with an alcohol swab.

FR Nettoyer la zone de prélèvement avec une compresse d'alcool.

ES Limpie la zona en la que utilizará la lanceta con un hisopo con alcohol.

PT Limpe a área a lancetar com uma zaragatoa com álcool.



2

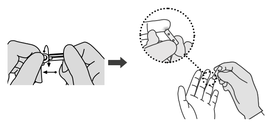
EN Squeeze the fingertip then prick the lateral side of the finger with a lancet provided. Wipe away the first blood drop. Then, safely dispose of the lancet immediately after.

FR Presser le bout du doigt et piquer le côté latéral du doigt avec une des lancettes fournies. Essuyer la première goutte de sang. Immédiatement après, jeter la lancette conformément aux règles de sécurité.

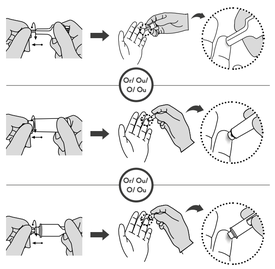
ES Apriete la punta del dedo y luego pinche el costado del dedo con la lanceta provista. Limpie la primera gota de sangre. Inmediatamente después, deseche la lanceta de manera segura.

PT Aperte a ponta do dedo e pique a lateral do dedo com uma lanceta fornecida. Limpe a primeira gota de sangue. Em seguida, elimine a lanceta em segurança imediatamente após a utilização.

[02FK16]



[02FK17]



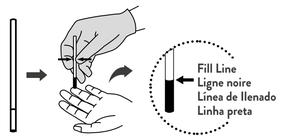
3

EN Immerse the open end of a new capillary pipette (10 µl) in the next blood drop and release the pressure to draw blood into the capillary pipette up to the fill line.

FR Immerger l'extrémité ouverte d'une pipette capillaire neuve (10 µl) dans la goutte de sang suivante, puis relâcher la pression pour aspirer le sang dans la pipette capillaire jusqu'au trait de remplissage.

ES Sumerja el extremo abierto de una nueva pipeta capilar (10 µl) en la siguiente gota de sangre y alivie la presión para introducir la sangre en la pipeta capilar hasta alcanzar la línea de llenado.

PT Com uma nova pipeta capilar (10 µL), mergulhe a extremidade aberta na gota de sangue seguinte e, em seguida, liberte a pressão para colher o sangue para a pipeta capilar até à marca.



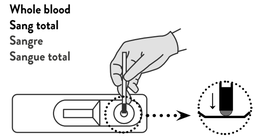
4

EN **Dispense 10 µl of drawn whole blood specimen** in the specimen well marked "S". Lightly touch the capillary pipette to the specimen pad while dispensing.

FR **Déposer 10 µl d'échantillon de sang total** prélevé dans le puits d'échantillon marqué « S ». Appuyer légèrement la pipette capillaire sur le tampon d'échantillon au moment de déposer l'échantillon.

ES **Deposite 10 µl de la muestra de sangre** extraída en el pocillo para muestras marcado con una "S". Al depositar la muestra, toque apenas la pipeta capilar con la almohadilla para muestras.

PT **Deite 10 µL de amostra de sangue total** colhida no poço de amostra marcado com "S". Toque ligeiramente com a pipeta capilar no bloco da amostra durante a dispensação.



5

EN Hold assay diluent bottle vertically and dispense 4 drops of assay diluent into the specimen well "S". Exactly, 4 drops should be added. Do not let bottle tip touch device in order to avoid cross-contamination.

FR **Tenir le flacon de diluant du test à la verticale et déposer 4 gouttes dans** le puits d'échantillon « S ». **Il faut ajouter très exactement 4 gouttes.** Ne pas mettre l'embout du flacon en contact avec le dispositif afin d'éviter toute contamination croisée.

ES **Sostenga la botella del diluyente del ensayo en forma vertical y deposite 4 gotas del diluyente** del ensayo en los pocillos para muestras "S". **Agregue exactamente 4 gotas.** No permita que la punta de la botella entre en contacto con el dispositivo a fin de evitar la contaminación cruzada.

PT **Mantenha o frasco de diluente do ensaio na posição vertical e deite 4 gotas de diluente** do ensaio no poço para o poço da amostra "S". **Devem ser adicionadas, exatamente, 4 gotas.** Não deixe a ponta do frasco tocar no dispositivo de modo a evitar a contaminação cruzada.

6

EN Interpret test results 5 - 20 minutes after adding assay diluent. Reading outside of this time frame (before 5 min or after 20 min) may provide false results.

FR Interpréter les résultats du test 5 à 20 minutes après l'ajout du diluant. Toute lecture en dehors de cette période (avant 5 minutes ou après 20 minutes) peut donner lieu à des résultats erronés.

ES Una vez transcurridos de 5 a 20 minutos de haber agregado el diluyente del ensayo, interprete los resultados. Leer el resultado fuera de ese marco de tiempo (antes de los 5 minutos o después de los 20 minutos) puede arrojar resultados falsos.

PT Interprete os resultados do teste 5 - 20 minutos após adicionar o diluente do ensaio. Efetuar a leitura fora deste intervalo de tempo (antes dos 5 minutos ou após os 20 minutos) pode fornecer resultados incorretos.

TEST INTERPRETATION / INTERPRÉTATION DU TEST / INTERPRETACIÓN DE LA PRUEBA / INTERPRETAÇÃO DO TESTE

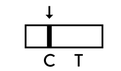
NON-REACTIVE / NON RÉACTIF / NO REACTIVO / NÃO-REATIVO

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

FR La présence de la ligne de contrôle uniquement (C) dans la fenêtre de résultat indique un résultat non réactif.

ES Si solo aparece la línea de control (C) en la ventana de resultados, el resultado es no reactivo.

PT A presença apenas da linha de controlo (C) dentro da janela de resultados indica um resultado não reativo.



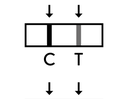
REACTIVE / RÉACTIF / REACTIVO / REATIVO

EN The presence of the test line (T) and the control line (C) within the result window, regardless of which line appears first, indicates a reactive result.
⚠ **Caution**: The presence of any test line, no matter how faint, the result is considered reactive.

FR La présence de la ligne de test (T) et de la ligne de contrôle (C) dans la fenêtre de résultat, quelle que soit la ligne apparue en premier, indique un résultat réactif.
⚠ **Mise en garde:** si la ligne de test est présente, même très pâle, le résultat est considéré comme réactif.

ES Si aparecen la línea de prueba (T) y la línea de control (C) en la ventana de resultados, independientemente del orden de aparición, el resultado es reactivo.
⚠ **Precaución:** La presencia de cualquier línea de prueba, aunque sea de un color débil, indica que el resultado es reactivo.

PT A presença da banda de teste (T) e da linha de controlo (C) dentro da janela de resultados, independentemente da linha que aparecer primeiro, indica um resultado reativo.
⚠ **Atenção:** a presença de qualquer linha de teste, mesmo sendo muito ténue, significa que o resultado é considerado reativo.



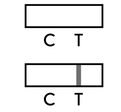
INVALID / NON VALIDE / NO VÁLIDO / INVÁLIDA

EN If the control line (C) is not visible within the result window after performing the test, the result is considered invalid. Instructions may not have been followed correctly or the test may have deteriorated. It is recommended that the specimen be retested using a new test device.

FR Si la ligne de contrôle (C) n'est pas visible dans la fenêtre de résultat après la réalisation du test, le résultat est considéré comme non valide. Il se peut que les instructions n'aient pas été suivies correctement ou que le test se soit détérioré. Il est recommandé d'analyser à nouveau l'échantillon à l'aide d'un nouveau dispositif de test.

ES Si no se ve la línea de control (C) en la ventana de resultados después de ejecutar la prueba, se considera que no hay un resultado válido. Esta situación puede deberse a que no se siguieron correctamente las instrucciones o a que la prueba se haya deteriorado. Se recomienda volver a analizar la muestra con un dispositivo de prueba nuevo.

PT Se a linha de controlo (C) não estiver visível dentro da janela de resultados após a realização do teste, o resultado é considerado inválido. As instruções podem não ter sido seguidas corretamente ou o teste pode ter-se deteriorado. Recomenda-se que a amostra seja novamente testada utilizando um novo dispositivo de teste.



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

Temperature limitation Limitation de température Límite de temperatura Limite de temperatura	LOT Lot Number No. de lot Número de Lote Número de lote	Manufacturer Fabricant Fabricante Fabricante	Do not use if package is damaged Ne pas utiliser si l'emballage est endommagé No utilizar si el envase está dañado Não utilizar se a embalagem estiver danificada
IVD For in vitro diagnostic use only Pour diagnostic in vitro uniquement Solo para uso de diagnóstico in vitro Somente para uso de diagnóstico in vitro	REF Catalogue number Numéro de référence Número de catálogo Número de catálogo	Date of manufacture Date de fabrication Fecha de fabricación Data de fabricaçao	Keep dry Conserver au sec Mantenganse seco Conservar seco
Do not reuse Ne pas réutiliser No Reutilizar Não reutilizar	Consult instructions for use Consulter le mode d'emploi Consulte las instrucciones de uso Consultar as instruções de utilização	Biological Risks Risques biologiques Riesgos biológicos Riscos biológicos	Caution Mise en garde Precaución Atenção
Use By Date de péremption Fecha de caducidad Utilizar até	Contains sufficient for (n) tests Permet de réaliser (n) tests Contenido suficiente para (n) pruebas Contém o suficiente para (n) testes	Keep away from sunlight Conserver à l'abri de la lumière du soleil Mantenganse fuera de la luz del sol Manter afastado da luz solar	