WHO Prequalification of In Vitro Diagnostics
PUBLIC REPORT

Product: SD BIOLINE HCV
WHO reference number: PQDx 0257-012-00

SD BIOLINE HCV with product codes **02FK10**, manufactured by **Standard Diagnostics, Inc.**, **Rest-of-World (RoW) regulatory version**, was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 29 November 2016.

Intended use:
SD 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. SD BIOLINE HCV is intended only for professional use 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. The performance of the assay has not been established for populations of infants or children.

Assay description:
SD BIOLINE HCV 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.

Test kit contents:

Component	**30 tests (product code 02FK10)**
Test devices with desiccant, in individual foil pouch	30T/kit
Assay diluent	1 x 5ml/vial
Instructions for use	1 unit

Items required but not provided:

Item
Precision pipette and tips
Protective gloves
Timer
Biohazard container

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

Shelf-life upon manufacture:
24 months.

Warnings/limitations:
As per 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.

Summary of WHO prequalification assessment for SD BIOLINE HCV

	Date	Outcome
PQ listing	29 November 2016	listed
Dossier review	18 October 2016	MR
Site inspection(s) of quality management system	21 January 2016	MR
Laboratory evaluation of performance and operational characteristics	8 August 2016	MR

MR: Meets requirements
N/A: Not applicable

Prioritization for prequalification
Based on the established criteria, SD BIOLINE HCV was given priority for WHO prequalification.

Product dossier assessment

Standard Diagnostics, Inc., submitted a product dossier for SD 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 will follow-up on implementation of these commitments at the next re-inspection.

Based on the product dossier assessment findings, the product dossier for SD BIOLINE HCV meets WHO prequalification requirements.

Manufacturing site inspection

A comprehensive inspection was performed at the site of manufacture (Production : 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 / Warehouse: 19-22, Dongtansandan 3-gil, Dongtan-myeon, Hwaseong-si, Gyeonggi-do 18487, Republic of Korea) between 6 to 8 May 2015 as per the "Information for manufacturers on prequalification inspection procedures for the sites of manufacture of diagnostics" (PQDx_014 v1). At the time of inspection, SD BIOLINE HCV was not inspected. 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. Therefore, SD BIOLINE HCV was deemed satisfactory according to WHO prequalification requirements.

The manufacturer's responses to the nonconformities found at the time of the inspection were accepted on 21 January 2016.

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

Laboratory evaluation

SD BIOLINE HCV was evaluated by WHO in the second quarter of 2016 using plasma specimens. From this evaluation, we drew the following conclusions, SD BIOLINE HCV assay is an immunochromatographic assay for the detection of antibodies to HCV in human serum, plasma and 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%	
Inter-reader variability %	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, capillary 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

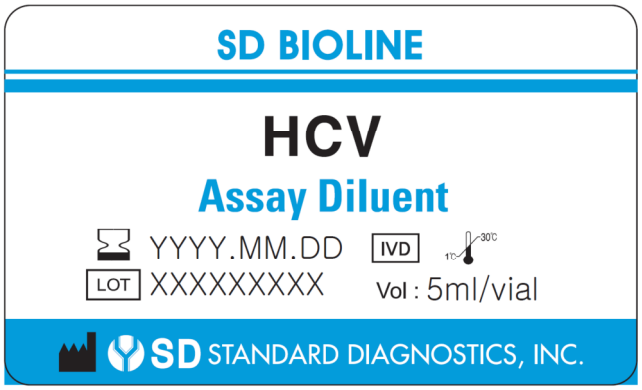
In-use stability of reagents	Until expiry date

Labelling

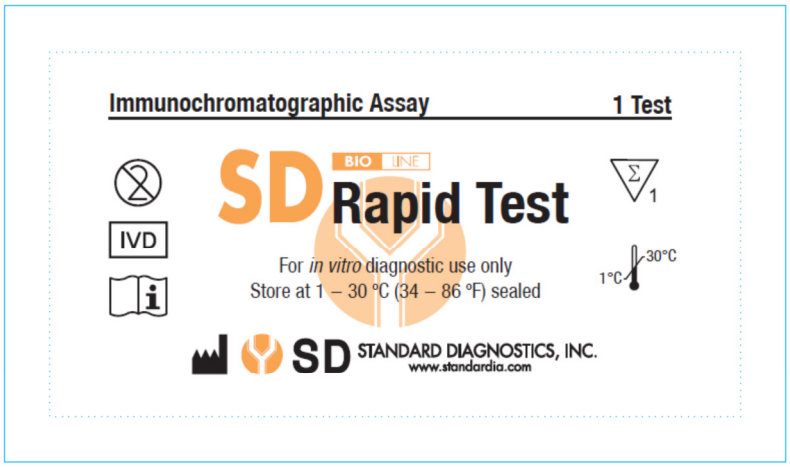
1. **Labels**
2. **Instructions for use**

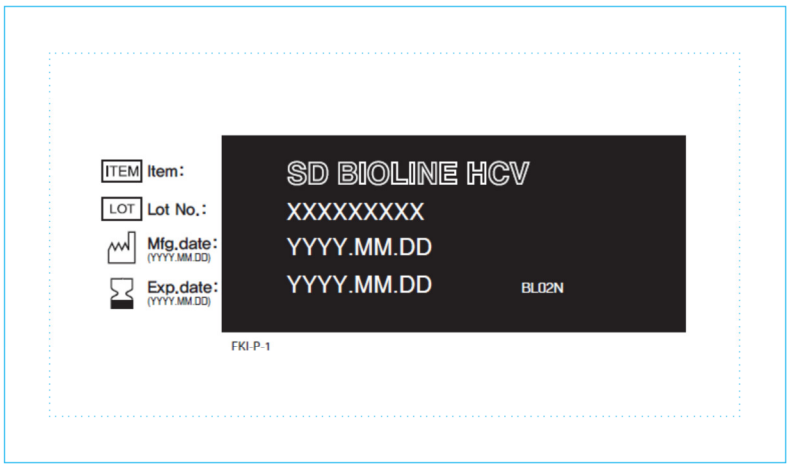
1. Labels

Assay diluent

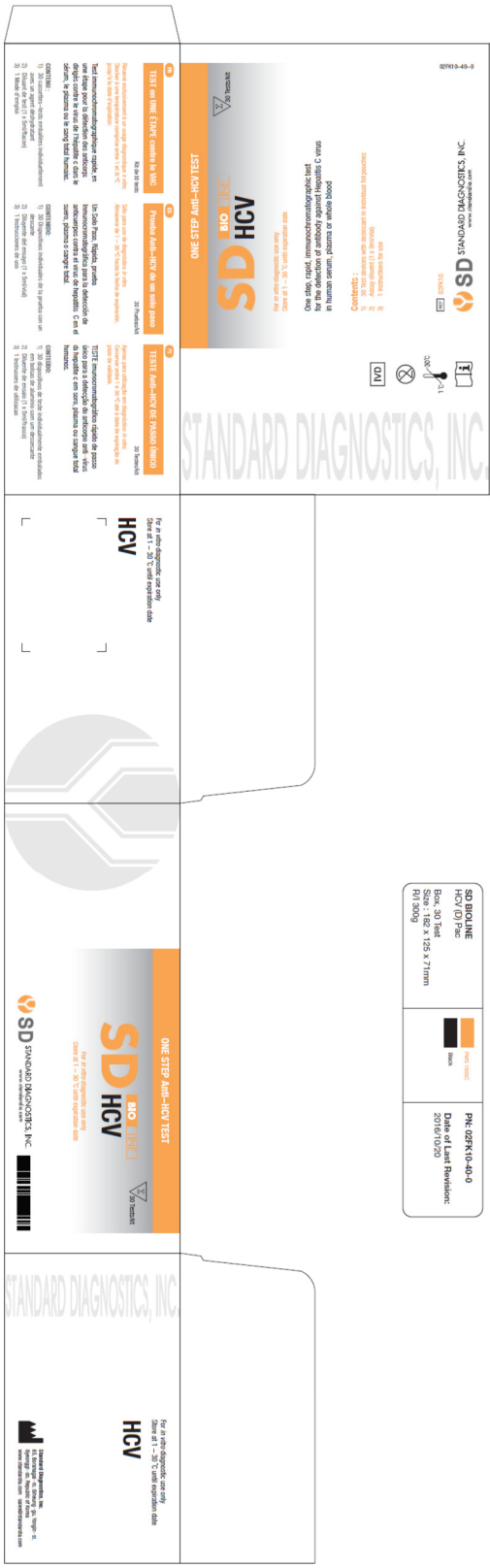


Device pouch





Package


ONE STEP Anti-HCV TEST
SD BIO LINE HCV
30 Tests/kit
STANDARD DIAGNOSTICS, INC.
SD BIOLINE
HCV (D) Pac
Box: 30 Test
Size : 182 x 125 x 71mm
N.W 300g
PN: 02FK10-40-0
Date of Last Revision:
2016/10/20

2. Instructions for use

ONE STEP of anti-HCV Test

SD BIO LINE HCV (02FK10)

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. SD 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 SD 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] SD 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 (heparin, EDTA and sodium citrate). SD 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. 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 SD BIOLINE HCV test kit contains the following items to perform the assay:
- 30 Test devices with desiccant in individual foil pouch
- Assay diluent (1 x 5ml/vial)
- 1 Instructions for use
2. Active ingredients of main components
- 1 Test device includes:
  - Gold conjugates: Protein A – gold colloid (1.0±0.2μg)
  - Test line: Recombinant HCV antigen (core, NS3, NS4, NS5) (1.5±0.3μg)
  - Control line: Goat anti-human Immunoglobulin (2.0±0.4μg)
- Assay diluent includes: 50 mM Tris-HCl Buffer (5ml), 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. Check the humidity indicator on the desiccant for color change and discard the pouch and the device if the color indicates saturation (OK if yellow. Discard if green). 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 pipette by mouth, smoke, drink, or eat 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 in 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.

Specimen collection and storage

1. Whole blood
- Using venipuncture, collect 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.

2. Plasma or serum
- [Plasma] By venipuncture collect 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] By venipuncture collect 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 (at -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 have 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. Allow 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 10μl of serum, plasma or whole blood specimen into the specimen well "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 SD 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 SD BIOLINE HCV test kit is designed to have 99.3 % (96.1 - 99.9 %) of sensitivity and 98.1 % (94.5 - 99.4 %) of specificity.
   A total of 299 serum specimens collected from Korea were tested on the SD 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		SD 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. SD BIOLINE HCV test kit has been evaluated in 3 different sites as below.

1) Study 1

A total of 1,187 serum specimens collected from Korea were tested on the SD 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 SD BIOLINE HCV were tested by the confirmatory assay using RT-PCR.

Reference assay		SD 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 SD BIOLINE HCV on all Anti-HCV positive specimens

	SD 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 SD 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 SD 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	SD BIOLINE HCV	
			Reactive	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 SD BIOLINE HCV.

- Sensitivity on seroconversion panels

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

Panel ID	SD 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 SD 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 SD 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

	SD 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 SD 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		SD 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 SD 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 SD 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).

3. Analytical performance

1) Analytical specificity

- 200/200 hospitalized patients were non-reactive on the SD BIOLINE HCV
- 200/200 specimens of pregnant women (incl. 20 specimens of multipara) were non-reactive on the SD BIOLINE HCV
- 100/100 specimens containing potentially cross reactive substances were non-reactive on the SD 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 SD 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 SD 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 SD BIOLINE HCV. All drugs were tested at concentrations of 250 µg/mL.

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

2) Prozone effect
SD BIOLINE HCV may exhibit prozone effect (false non-reactive result) in specimens which have higher than S/CO of approx. 11.0 in Abbott Architect and S/CO 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 SD 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 SD BIOLINE HCV reactive/No. of positive specimens	No. of SD 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 1 to 4 days at 4°C.
Table 5. Result obtained on spiked fresh specimens

		SD BIOLINE HCV	
		Reactive	Non-reactive
25 negative specimens	day 0	0	25
25 negative specimens spiked with anti-HCV	day 0	25	0
	day 1	25	0
	day 2	25	0
	day 3	25	0
	day 4	25	0

5) Reproducibility of the SD 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.

Bibliography of suggested reading

1. Arash G., Czeslaw W., Chao Lin, Stephen M. Feinstone, and Charles M. Rice : Expression and Identification of Hepatitis C Virus Polyprotein Clevage 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. Griva, F. Garetto, R. Calogero, 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

Glossary of Symbols

IVD	*In vitro* diagnostic medical device		Manufacturer
	Do not re-use		
	Consult instructions for use	LOT	Batch code
	Temperature limitation	REF	Catalogue number
	Use by : Exp	Σ n	Contains sufficient for <n> tests

Product Disclaimer:
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 diagnosis using this product.

Date Issued : 2016. 11
02FK10-01-En-3

Manufactured by
SD STANDARD DIAGNOSTICS, INC.
65, Borahagal-ro, Giheung-gu, Yongin-si, Gyeonggi-do, Republic of Korea
Tel : 82-31-899-2800 Fax : 82-31-899-2840
http://www.standardia.com sales@standardia.com

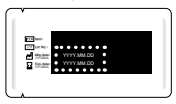
Preparation

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

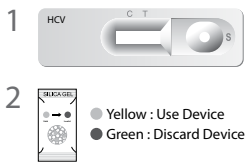
1
Carefully read the instructions on how to use the SD BIOLINE HCV test kit.

2
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.

[For example]



3

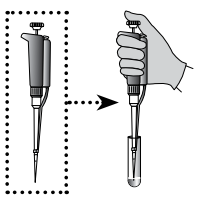


Open the foil pouch and look for the following:
1. Test device
2. Desiccant

Then, label the device with the patient identifier.

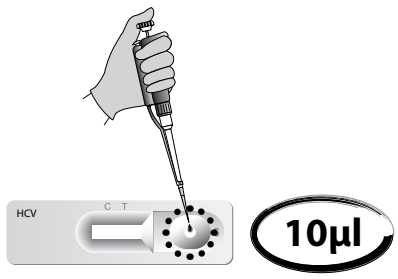
Test procedure

Specimen collection



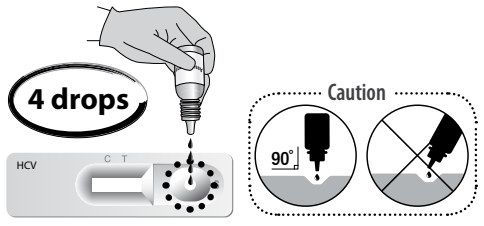
Take **10µl of serum, plasma or whole blood specimen** using a micropipette.

1



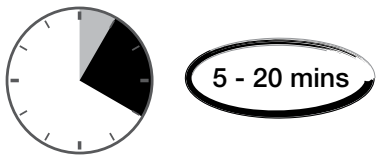
Dispense 10µl of serum, plasma or whole blood specimen into the specimen well "S".

2



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.

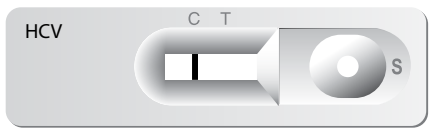
3



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.

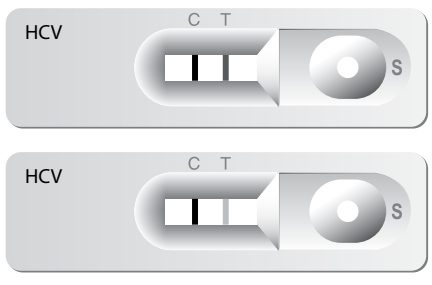
Test interpretation

Non-reactive



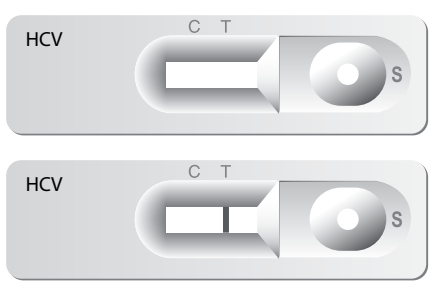
The presence of only the control line (C) within the result window indicates a non-reactive result.

Reactive



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



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 beyond the expiration date. It is recommended that the specimen be retested using a new test device.