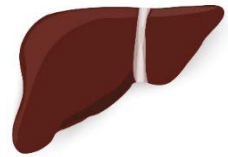
SD BIOLINE Hepatitis C Virus Training

Contents

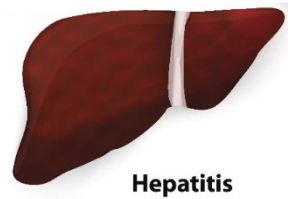
Hepatitis C Overview

What is Hepatitis?

- A medical condition defined by the inflammation of the liver and characterized by the presence of inflammatory cells in the tissue of the organ[1].
- There are 6 viruses known to affect the liver and cause Hepatitis: HAV, HBV, HCV, HDV (Delta), Hepatitis E virus (HEV) and HGV[1].
- Hepatitis A and E are typically caused by ingestion of contaminated food or water[1].
- Hepatitis B, C and D are typically caused by contact with contaminated blood or body fluids[1].
- There are two chronic and serious forms[1]:
  - Hepatitis B
  - Hepatitis C



Normal liver



Hepatitis

Data adapted from: 1. http://www.who.int/mediacentre/factsheets/fs164/en/

HCV Virus - Overview

Parameter	HCV
Genome	ssRNA
Incubation Period	15-150 days
Transmission	Blood borne
Carrier State	50-70%
Chronic Hepatitis	>50%
Hepatocellular Mortality*	1-2%
Vaccination	Currently not available
Treatment	Simple. DAA(90 day regime)

Data adapted from: 2. https://www.cdc.gov/hepatitis/hcv/cfaq.htm#overview

HCV Overview and the Unmet Need

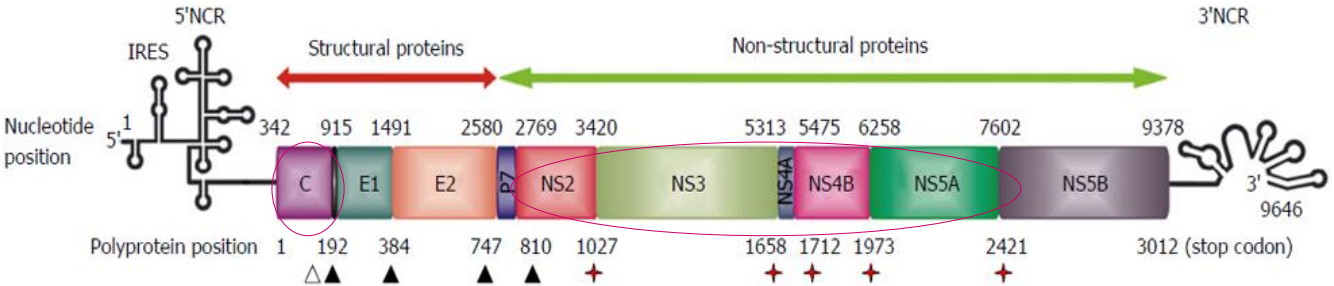
- Globally, 130–150 million people have chronic hepatitis C infection[3]
- Approx. 700,000 people die each year from hepatitis C-related liver diseases[3]
- Most people infected with HCV are not aware they are infected; therefore, HCV is called the "silent pandemic" or "silent killer"[4]
- Of those with chronic HCV infection, the risk of cirrhosis of the liver is 15-30% within 20 years[4]
- There is NO vaccine against HCV...yet
- An early diagnosis in the course of the disease can:
  - Increase the chances of successful treatment
  - Increase impact of essential lifestyle changes
  - Limit cross-infection
- Many POC tests currently on the market are old and with sub-optimal performance
- POCTs of blood have the highest accuracy, followed by RDTs of serum or plasma and then by POCTs of oral fluids[5]

Source adapted from 3. WHO HCV Fact sheet Read here
Source adapted from 4: WHO June 2016 – Global Health sector Strategy on Viral hepatitis 2016-20121
Source adapted from 5: Shivkumar *etal* .- Accuracy of Rapid and Point-of-Care Screening Tests for Hepatitis C. Khuroo et al Diagnostic Accuracy of Point-of-Care Tests for Hepatitis C Virus Infection: A Systematic Review and Meta-Analysis

Hepatitis C Virus

An envelope, single stranded positive sense RNA including:

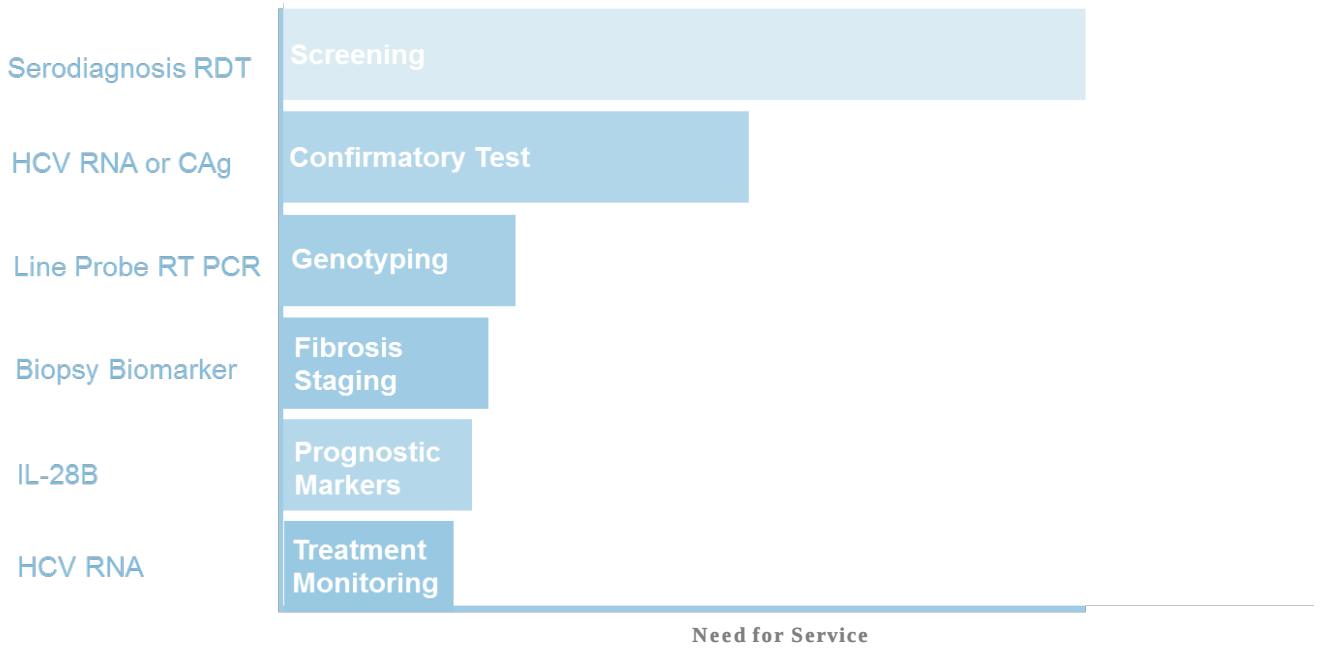
- Structural genes at the 5' end
- Non-structural genes at the 3' end



Data adapted from: 6. Echeverría N, Moratorio G, Cristina J, Moreno P. Hepatitis C virus genetic variability and evolution. *World J Hepatol* 2015; 7(6): 831-845

The HCV Diagnosis Continuum

The Hepatitis C Virus is a complex organism and treatment modalities are varied.



Data adapted from: 7. Figure adapted from: 2. UNIT AID (2015) Hepatitis C – Diagnostics Technology Landscape 1st Edition.

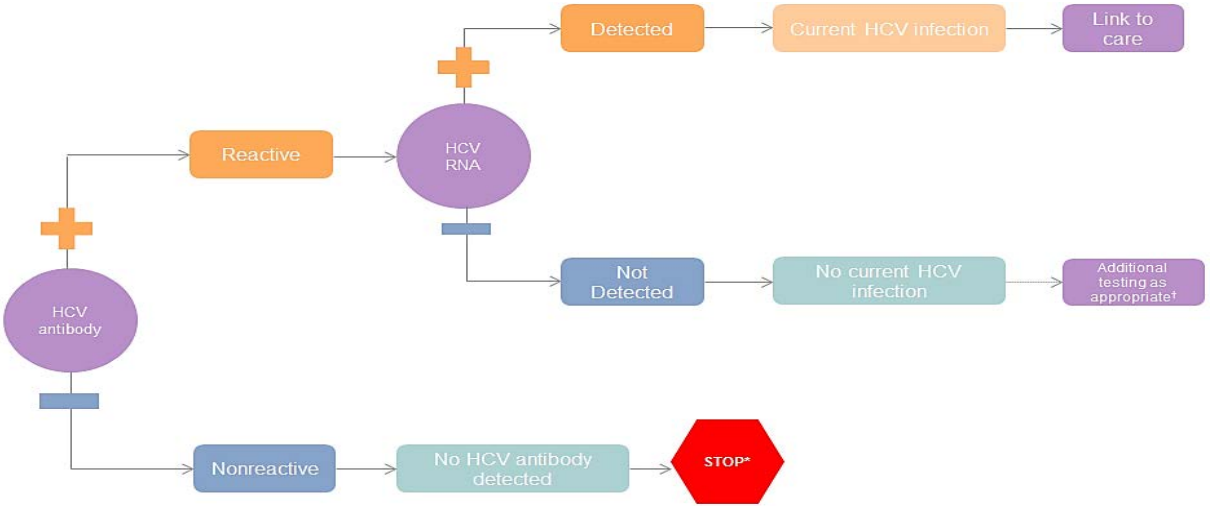
Hepatitis C Antibody Testing

Antibody Test Development History

HCV BIOLINE Product	First Generation	Second Generation	Third Generation
Performance	• Limited sensitivity and specificity	• Remarked improvement in sensitivity and specificity • To avoid nonspecific cross-reactivity	• Improved sensitivity • Shorten the window
Reagents	• NS4	• Core • NS3 • NS4	• Core • NS3 • NS4 • NS5
Window Period	• 3-4 months	• 8-12 weeks	• 6-10 weeks

Data adapted from: 8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3943138/

Common Hepatitis C Virus Testing Algorithm



* For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody is recommended. For persons who are immunocompromised, testing for HCV RNA can be considered.
† To differentiate past, resolved HCV infection from biologic false positivity for HCV antibody, testing with another HCV antibody assay can be considered. Repeat HCV RNA testing if the person tested is suspected to have had HCV exposure within the past 6 months or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.

Data adapted from: 9. Getchell, Jane P. *et al.* (2013) Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report. Testing for HCV Infection: An Update of Guidance for Clinicians and Laboratorians. Weekly Vol. 62 No. 18. 19-20.

HCV Test Interpretation Table

Test Outcome	HCV antibody nonreactive	HCV antibody reactive	HCV antibody reactive, HCV RNA detected	HCV antibody reactive, HCV RNA not detected
Interpretation	No HCV antibody detected	Presumptive HCV infection	Current HCV infection	No current HCV infection
Further Action	Sample can be reported as nonreactive for HCV antibody. No further action required. If recent HCV exposure in person tested is suspected, test for HCV RNA.[1]	A repeatedly reactive result is consistent with current HCV infection, or past HCV infection that has resolved, or biologic false positivity for HCV antibody. Test for HCV RNA to identify current infection.	Provide person tested with appropriate counseling and link person tested to medical care and treatment.[2]	No further action required in most cases. If distinction between true positivity and biologic false positivity for HCV antibody is desired, and if sample is repeatedly reactive in the initial test, test with another HCV antibody assay. In certain situations[3] follow up with HCV RNA testing and appropriate counseling.

Data sourced from: 9.Getchell, Jane P. *et al.* (2013) Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report. Testing for HCV Infection: An Update of Guidance for Clinicians and Laboratorians. Weekly Vol. 62 No. 18. 19-20.

WHO- HCV Screening Recommendations

Testing approach and population	Recommendations*
Focused testing in most affected Populations	• Adults and adolescents from populations most affected by HCV infection2 (ie. who are either part of a population with high HCV seroprevalence or who have a history of exposures and/or high-risk behaviours for HCV infection) • Adults and children with a clinical suspicion of chronic viral hepatitis3 (ie.symptoms, signs, laboratory markers).
General population testing	In settings with a ≥2% or ≥5% 4 HCV antibody seroprevalence in the general population it is recommended that all adults have access to and be offered HCV serological testing
Birth cohort testing	This approach may be applied to specific identified birth cohorts of older persons at higher risk of infection6 and morbidity within populations that have an overall lower general prevalence.

Data sourced from: 10. WHO GUIDELINES ON HEPATITIS B AND C TESTING December 2016

HIV/HCV Co-infection

- HIV increases the levels of HCV viremia and progression to cirrhosis, liver failure and death.
- Risk of liver-related mortality in the co-infected is related to HIV viral load and CD4 count.

For more information:

- Accelerated clinical progression of HIV-1 (*Mathurin et al., 1998; Tong, El-Farra, Reikes& Co, 1995)*
- Impaired CD4-cell recovery and faster HIV disease progression in HCV co-infected patients despite their receiving ART *(Grueb, 2000)*
- No impact on CD4 count, viral load, HIV progression or survival *(Hayashi et al, 1991; Thomas et al., 1996; Mayor, 2006; Merriman et al., 2006)*

SD BIOLINE HCV

- Immunochromatographic assay
- Test for the qualitative detection of antibodies specific to HCV in human WB, serum or plasma
  - Sensitivity : 99.3%
  - Specificity :98.1%
  - 24months at 1-30°C
- Recombinant HCV capture antigen as Core, NS3, NS4 and NS5.
- Specimen : Serum, Plasma, Whole blood 10ul
- WHO PQ CE*

*WHO PQed Cat. No. : 02FK10, 02FK16 and 02FK17 | CE Cat. No. : 02FK10CE | 02FK11 and 02FK12 don't belong any PQ or CE

Data adapted from: 12. SD BIOLINE HCV package insert

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 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.

Data adapted from: 12. SD BIOLINE HCV package insert

SD BIOLINE HCV Kits

Components*	Catalogue Number (s)		
	02FK10	**02FK16**	**02FK17**
Specimen Procedure(s)	Serum, plasma and whole blood (venous WB and finger-prick blood)		
Test devices (in individual foil pouch)	30 T/kit	25 T/kit	25 T/kit
Assay Diluent	1 x 5 ml/vial	1 x 5 ml/vial	1 x 5 ml/vial
Capillary Pipette(s)	NA	25 (10 µl each)	25 (10 µl each)
Sterile Lancet(s)	NA	25	25 (safety lancet)
Alcohol swab(s)	NA	25	25

Data adapted from: 12. SD BIOLINE HCV package insert

SD BIOLINE HCV Clinical Performance*

Study Background	# of samples	Specificity	Sensitivity	Reference Method
1) Serum Samples from Korea Specimens were tested on the SD BIOLINE HCV. Specimens confirmed by a leading commercial anti HCV ELISA test.	142 (Anti-HCV Pos.) 157 (Anti-HCV Neg.) **Total: 299**	98.1% (154/157)	99.3% (141/142)	ELISA
Additional Clinical Studies				
2) Serum Samples from Korea Specimens were tested on the SD BIOLINE HCV. Specimens confirmed by a leading commercial anti HCV ELISA test.	157 (Anti-HCV Pos.) 1030 (Anti-HCV Neg.) **Total: 1187**	99.4% (1024/1030)	100% (157/157)	ELISA

Data adapted from: 12. SD BIOLINE HCV package insert

SD BIOLINE HCV Clinical Performance*

Study Background	# of samples	Specificity	Sensitivity	Reference Method
3) WHO Laboratory Evaluation Clinically derived serum/plasma specimens from Australia, Europe, Africa, Latin America & Asian origins.	163 (Anti-HCV Pos.) 320 (anti-HCV Neg.) **Total: 483**	100% (320/320)	100% (163/163)	Confirmed by commercial EIA test
4) Diagnostic Sensitivity (CE study) European performance evaluation (German Red Cross and Sanquin, Netherlands).	213 (Anti-HCV Pos.) serum/plasma 100 (Anti-HCV Pos.) Whole Blood 97 (Anti-HCV Pos.), known genotype **Total: 410**		99.3%	▪ 213 specimens confirmed with CHIRON HCV RIBA™ 3.0 SIA or INNO-LIA HCV Score ▪ 100 paired WB and plasma specimens were tested with Abbott Architect anti-HCV ▪ 94 specimens with known genotype 1 to 6, based on the VERSANT HCV Genotype 2.0 (LiPA)
5) Diagnostic Specificity (CE study) Specimens from blood donors negative for anti-HCV with ABBOTT PRISM were tested collected from Germany.	1000 plasma 500 whole blood (Anti-HCV Neg.) **Total: 1500**	100%		Abbott Prism

Data adapted from: 12. SD BIOLINE HCV package insert

SD BIOLINE HCV Clinical Performance**
Finger Prick Performance vs Other Sample Types

Four types of blood (serum, plasma, venous whole blood and finger prick blood) were collected from 243 persons in Bangladesh.

- Finger prick blood specimen showed 99.6% (242/243) agreement with other specimen types.
- There was only one discordance specimen. This specimen was further confirmed as weak positive by a commercial anti-HCV assay.

Specimen Type		Finger Prick Blood		
		POS	NEG	Total
Serum, Plasma, Venous Whole Blood	POS	85	1*	86
	NEG	0	157	157
	Total	85	158	243
Agreement (95% CI)		99.6% (97.7% – 99.9%)		

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

Data adapted from: 12. SD BIOLINE HCV package insert

WHO Prequalification: SD BIOLINE HCV Kit

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.
- This report was further amended on 26 March 2018 to reflect the addition of specimen collected from finger prick, and subsequently two additional product formats with product codes 02FK16 and 02FK17.

Data adapted from: 13. http://www.who.int/diagnostics_laboratory/evaluations/pq-list/hcv/180326_amended_final_pqpr_0257_012_00.pdf?ua=1

WHO Laboratory Evaluation

Study Background	# of samples	Specificity	Sensitivity	Reference Method
WHO Laboratory Evaluation* Clinically derived serum/plasma specimens from Australia, Europe, Africa, Latin America & Asian origins.	163 (Anti-HCV Pos.) 320 (anti-HCV Neg.) **Total: 483**	100% (320/320)	100% (163/163)	Confirmed by commercial EIA test

Change notification:
Standard Diagnostics, Inc., submitted a change notification on 21 September 2017 to reflect the addition of specimen collected from finger-prick and subsequently two additional product codes (02FK16 and 02FK17). The change request was assessed and found to be acceptable on 10 January 2018.

* Performance characteristics in comparison with an agreed reference standard (final study)

Data adapted from:13. http://www.who.int/diagnostics_laboratory/evaluations/pq-list/hcv/180326_amended_final_pqpr_0257_012_00.pdf?ua=1

SD BIOLINE HCV Clinical Performance (CE)**

Study Background	# of samples	Specificity	Sensitivity	Reference Method
Diagnostic Sensitivity (CE study) European performance evaluation (German Red Cross and Sanquin, Netherlands).	213 (Anti-HCV Pos.) serum/plasma 100 (Anti-HCV Pos.) Whole Blood 97 (Anti-HCV Pos.), known genotype **Total: 410**		99.3%	▪ 213 specimens confirmed with CHIRON HCV RIBA™ 3.0 SIA or INNO-LIA HCV Score ▪ 100 paired WB and plasma specimens were tested with Abbott Architect anti-HCV ▪ 94 specimens with known genotype 1 to 6, based on the VERSANT HCV Genotype 2.0 (LiPA)
Diagnostic Specificity (CE study) Specimens from blood donors negative for anti-HCV with ABBOTT PRISM were tested collected from Germany.	1000 plasma 500 whole blood (Anti-HCV Neg.) **Total: 1500**	100%		Abbott Prism

** The detailed information available in the package insert.

References

1. http://www.who.int/mediacentre/factsheets/fs164/en/
2. https://www.cdc.gov/hepatitis/hcv/cfaq.htm#overview
3. WHO HCV Fact sheet Read here
4. WHO June 2016 – Global Health sector Strategy on Viral hepatitis 2016-20121
5. Shivkumar *etal* .- Accuracy of Rapid and Point-of-Care Screening Tests for Hepatitis C. Khuroo et al Diagnostic Accuracy of Point-of-Care Tests for Hepatitis C Virus Infection: A Systematic Review and Meta-Analysis
6. Echeverría N, Moratorio G, Cristina J, Moreno P. Hepatitis C virus genetic variability and evolution. *World J Hepatol* 2015; 7(6): 831-845
7. Figure adapted from: 2. UNIT AID (2015) Hepatitis C – Diagnostics Technology Landscape 1st Edition.
8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3943138/
9. Getchell, Jane P. *et al.* (2013) Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report. Testing for HCV Infection: An Update of Guidance for Clinicians and Laboratorians. Weekly Vol. 62 No. 18. 19-20.
10. WHO GUIDELINES ON HEPATITIS B AND C TESTING December 2016
11. Accelerated clinical progression of HIV-1 (*Mathurin et al., 1998; Tong, El-Farra, Reikes & Co, 1995) Slide 20*
12. SD BIOLINE HCV package insert
13. http://www.who.int/diagnostics_laboratory/evaluations/pq-list/hcv/180326_amended_final_pqpr_0257_012_00.pdf?ua=1


Abbott