Hepatitis C Market Memo
July 2022

The Clinton Health Access Initiative (CHAI) published its **first** and **second** editions of the *HCV Market Intelligence Report* in May 2020 and August 2021 covering market updates for 2019 and 2020, respectively. This memo serves as an interim update on the market for hepatitis C virus (HCV) diagnostics and treatment, providing key updates on supply and pricing trends from January 2021 to April 2022. The release of an interim hepatitis B market update is planned for later this year and the third edition of CHAI's *Hepatitis Market Intelligence Report* is planned for 2023.

WHO Prequalified Products

There remains a robust availability of quality-assured products, with four rapid diagnostic tests (RDT), four lab-based immunoassays, four viral load (VL) assays, and 13 generic direct acting antiviral (DAA) products retaining World Health Organization Prequalified (WHO PQ'd) status and several under assessment. However, this year brought some changes, with a few diagnostic and drug suppliers not retaining their PQ status.

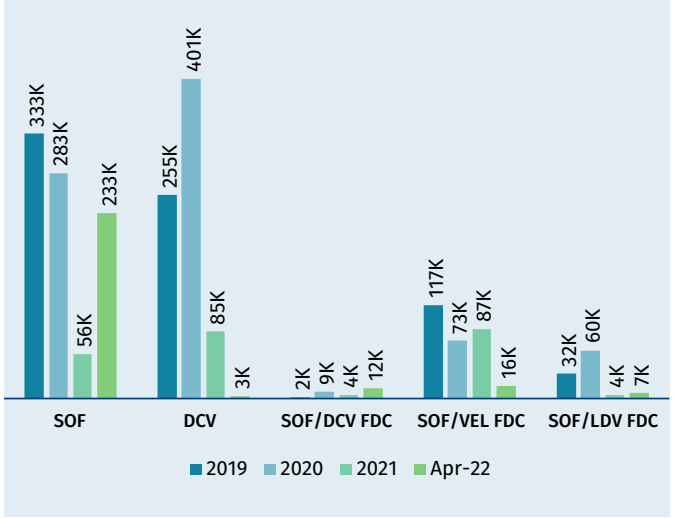
HCV RDT	Under Assessment	Three new HCV RDTs are undergoing the WHO PQ process
Lab-based immunoassay	Not Retained	DiaSorin South Africa and Biokit South Africa's HCV products are no longer WHO PQ'd
Viral load assay	Under Assessment	Cepheid's Xpert HCV VL Fingerstick
	Not Retained	Genedrive did not retain WHO PQ for their viral load assay
DAAs	Under Assessment	One generic SOF/VEL product
	Not Retained	SOF/LDV FDC and DCV (30mg) by Viatris and SOF (400mg) by Cipla are no longer WHO PQ'd

The cost of maintaining PQ status being higher than the return on sales may have driven the decision to not retain PQ by some suppliers. For the list of PQ'd treatment products, please refer to Exhibit 14 in the 2021 HCV Market Intelligence Report. For an updated list of PQ'd diagnostic products, please refer to WHO Public Reports for In Vitro Diagnostics (Hepatitis C Assays).

Volume Trends

In 2021, DAA procurement volumes from India, a major DAA supplier, continued to decrease amidst recurring surges in COVID-19 infections and disruptions to health services. Countries are continuing to adapt and reinvest in scaling hepatitis C programs.

2019-2022: Indian Generic DAA Packs Exported to LMICs



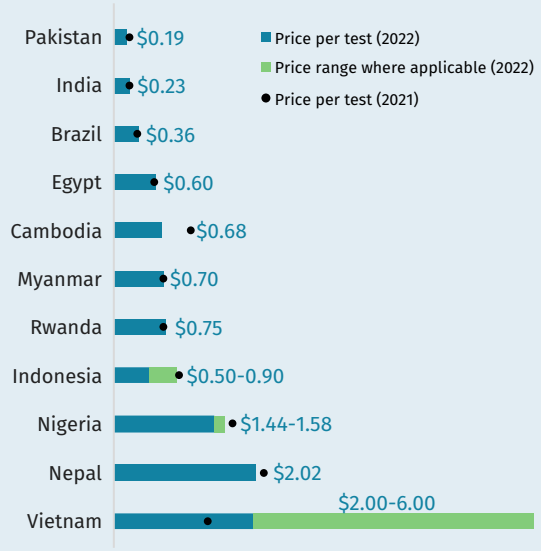
- While DAA export volumes decreased by 71% in 2021, early procurement trends of 2022 show a sign of recovery driven by substantial sofosbuvir (SOF) procurement by Pakistan.
- 2021 DAA export volumes were less than 20% of their average pre-pandemic levels. A major driver of this decline was the decrease in demand from Rwanda, Pakistan, Ukraine, and Nigeria, which had driven an increase in procurement volumes over the last 3 years.
- The decline in 2021 demand can be attributed to geo-political instability in some regions, COVID-19-related program disruptions, and some HCV programs nearing elimination.

Continued scale-up of hepatitis testing and treatment services is required to meet the substantial remaining need for HCV treatment—more than 50 million patients remain untreated worldwide.

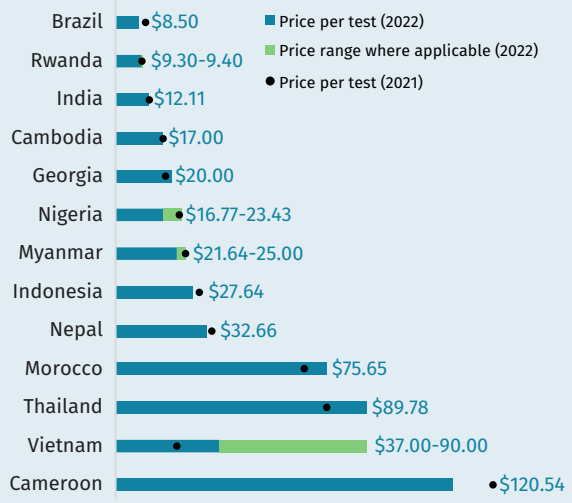
Diagnostic Pricing Trends

Prices of HCV diagnostic tests, for both RDT and VL, have remained relatively stable across most high-burden countries.

Costs of HCV Antibody RDTs in Public Programs within a Sample of High-Burden Countries (USD)



Cost of HCV VL Paid by Public Programs within a Sample of High-Burden Countries (USD)

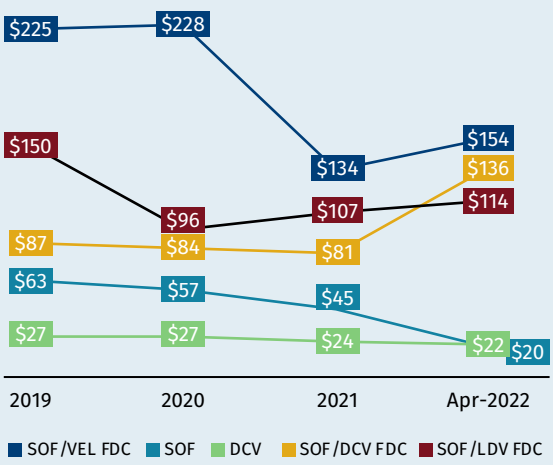


DAA Pricing Trends

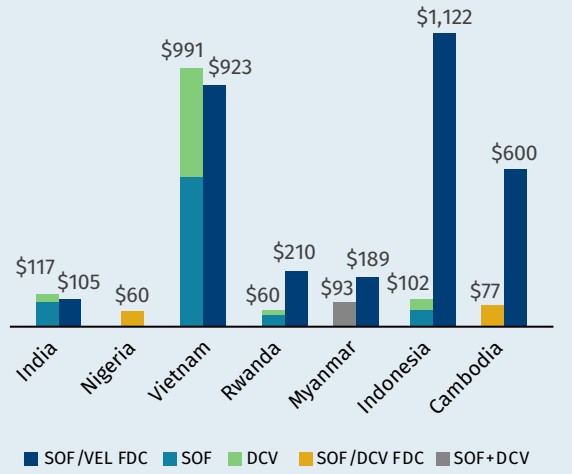
While DAA prices remain largely stable on average, Nasarawa State in Nigeria achieved a significant price decrease of 55% to a price of US$60 for 12 weeks treatment course.

- The average Freight on Board (FOB) price of most generic DAAs fell marginally between 2020-2022; SOF/VEL FDC FOB prices declined significantly by over 30% in this period.
- Nasarawa state in Nigeria secured a price of US$60 (55% reduction) for a 12-week course of the SOF and DCV through continuous state government investment in the scale-up of hepatitis care, optimization of in-country margins, and collaboration with manufacturers.

Weighted Average FOB Price for 12 Weeks Treatment Course of DAAs In LMICs from 2019- 2022 (USD)



In-Country Prices of DAAs for 12 Weeks Treatment Course (USD)



- HCV drug list in GFATM framework agreements now includes SOF/VEL FDC.
- GFATM revised its reference prices for hepatitis drugs in February 2022 with a marginal reduction in prices of DAAs.

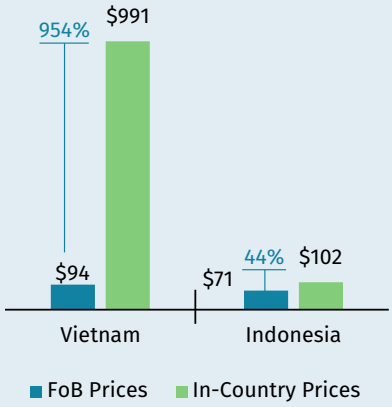
Negotiated Prices by GFATM & PAHO for 12 Weeks of Treatment

Mechanism	Eligible countries	DAAs	Price for 12-week treatment	Change from prev. agreement
GFATM	List	SOF+DCV	US$ 85.5	-US$ 3.5
		SOF/DCV FDC	US$ 74.45	-US$ 0.55
		SOF/LDV FDC	US$ 78.75	-US$ 0.25
		SOF/VEL FDC	US$ 174	
PAHO	List	SOF+DCV	US$ 102	
		SOF/VEL FDC	US$ 4050	

High In-Country Pricing Continues to Inhibit HCV Program Scale-Up

- Despite a significant reduction in DAA prices, the final price to program/patients remains high and unaffordable in some countries.
- Price markups, which typically include insurance costs, in-country taxes and duties, logistic costs, and distributor margins, result in a two- to ten-fold increase over the FOB price.
- More affordable pricing may be achieved through identifying components of in-country mark-ups and devising strategies to limit them. Some methods to achieve mark-up reductions include imposing limits on fee charges, streamlining in-country procurement mechanisms, facilitating a competitive tendering process for distribution/logistics partners, and optimizing in-country supply chains.

In-Country Price Markup (USD) for 12 Weeks Treatment Course of SOF + DCV (Indicative)



Emerging Market Trends

Expanding access to testing and pediatric treatment have emerged as new frontiers in the HCV diagnostics and treatment markets.

HCV Self-Testing (HCVST):

- In July 2021, WHO released guidance on HCVST as an additional approach for HCV testing services, particularly for populations who may experience barriers when accessing testing in traditional healthcare settings.
- The market for HCVST is nascent as manufacturers continue to conduct evaluations for self-testing. Three manufacturers now offer research-use-only (RUO) HCVST products.

HCV Self-Test Products Available for Research Use

Product name	Manufacturer	Sample type	Anticipated Pricing
OraQuick HCV Rapid Antibody Self-Test*	OraSure Technologies	Oral fluid	NA
First Response HCV Card Test (Self-Test)*	Premier Medical Corporation (PMC)	Whole blood (fingerstick)	US$ 1.75-2
Wondfo HCV Self-Test*	Wondfo Biotech Co., Ltd	Whole blood (fingerstick)	NA

**Products are undergoing evaluations needed for regulatory assessment*

Simplified Service Delivery and HCV Viral Load Testing:

Recently released update of **WHO guidelines** recommends increasing access to testing and treatment through **decentralization** to lower-level health facilities and community-based venues; **integration** with existing care services such as in primary care, harm reduction programs, prisons, and HIV services; and **task sharing** with trained non-specialists. As such, recommendations around viral load include:

- **Point-of-care HCV RNA assays** can be used as an alternative approach to laboratory-based HCV RNA to diagnose viremia and as an alternative approach for test of cure. Currently the Xpert HCV Viral Load test has PQ and can be used near point of care with Cepheid GeneXpert systems using plasma or serum samples; a version using whole blood is undergoing PQ assessment.
- **Reflex HCV viral load testing** can increase linkage to care and treatment. Through a lab-based approach, reflex viral load testing includes performing confirmation of viremia on a sample already in a lab. Alternatively using a clinic-based approach, reflex viral load testing includes immediate sample collection to conduct the HCV viral load, following a positive HCV antibody RDT result.

*Please refer to Exhibit 4 and 9 of **2021 HCV Market Intelligence Report** for more information on VL products and pricing.*

Pediatric Market:

- Recently released update of **WHO guidelines** on HCV testing and treatment has expanded the DAA market by recommending pangenotypic DAA regimens for adolescents and children aged three years and above with hepatitis C infection, regardless of the stage of the disease. Treatment of children less than three years old is not recommended due to the high rate of spontaneous viral clearance in young children.
- 200 mg of SOF was recently included on the WHO Model List of Essential Medicines for Children in September 2021.

While 200 mg of SOF is the recommended dose in younger children, due to the challenges that small children face with swallowing tablets, a regimen comprising two 100 mg SOF tablets rather than a single 200 mg SOF tablet is preferred.

Development of preferred 100 mg SOF tablet from generics is now needed to treat children with HCV. CHAI estimates an addressable market of approximately 500,000 children requiring pediatric formulations across seven countries with robust adult HCV programs (**see 2021 HCV Market Intelligence Report**).

Recommended WHO Guidelines for HCV Treatment for Adults, Adolescents, and Children

	Pangenotypic DAA Regimens		
	SOF/DCV[1]	SOF/VEL[5]	G/P[3]
Dosing by weight	**>26 kg**: 400/60 mg	**> 30 kg**: 400/100 mg	**> 45 kg**: 300/120 mg
	14-25 kg: 200 mg/30 mg[1,2]	**17-29 kg**: 200/50mg	**30-45 kg**: 250/100 mg **20-<30 kg**: 200/80 mg
		<17 kg: 150/37.5mg	**<20kg**: 150/60 mg
Duration	12 weeks across age groups[4]	12 weeks across age groups	8 weeks across age groups

1 Dosing based on population pharmacokinetic modelling studies; 2 SOF is preferred as 100 mg tablet for children; 3 Available as tablets (FDC) 100/40 mg or granules 50/20 mg; 4 In those without cirrhosis. Treatment for 24 weeks is recommended in those who are treatment-experienced or with compensated cirrhosis; 5 Available as tablet (FDC) or granules

Data Sources:

- WHO PQ
- India Export Data 2021 and 2022 (Until April)
- GFATM Reference Pricing
- PAHO Price List
- CHAI Supported Country Teams
- CHAI Analysis
- MapCrowd Database
- WHO recommendations for Service Delivery & Diagnostics for HCV infection
- WHO recommendations for treatment of adolescents and children with chronic HCV infection

Acronyms Used:

Ag	Antigen
CE	Conformitè Europëenne
CHAI	Clinton Health Access Initiative
DAA	Direct Acting Antivirals
DCV	Daclatasvir
ERP	Expert Review Panel
ERPD	Expert Review Panel for Diagnostics
FDA	U.S. Food and Drug Administration
FDC	Fixed Dose Combination
FOB	Freight on Board
GFATM	The Global Fund to Fight AIDS, Tuberculosis and Malaria
HCV	Hepatitis C Virus
HCVST	Hepatitis C Virus Self-Testing
IVD	In-vitro Diagnostics
LMICs	Low-and Middle-Income Countries
NA	Not Available
PAHO	Pan American Health Organization
PQ	Prequalification
PQ'd	Pre-qualified
RDT	Rapid Diagnostic Test
RNA	Ribonucleic Acid
RUO	Research Use Only
SOF	Sofosbuvir
SOF + DCV	Sofosbuvir and Daclatasvir used in combination
SOF/DCV	Sofosbuvir/Daclatasvir
SOF/DCV FDC	Sofosbuvir/Daclatasvir Fixed-Dose Combination
SOF/LDV FDC	Sofosbuvir/Ledipasvir
SOF/VEL FDC	Sofosbuvir/Velpatasvir
SRA	Stringent Regulatory Authorities
VL	Viral Load
WHO	World Health Organization

Notes:

1. India export data does not account for the use or export of DAAs manufactured outside India, procurement within India, or sales or donations by originators.
2. All data in this update is until April 2022.
3. Correction from previous HCV Market Intelligence report 2021—Orasure's product OraQuick HCV Rapid Antibody Test can use the following sample types: oral fluid, fingerstick and venous whole blood, serum, and plasma.

Pricing:

- FOB and in-country prices are for both WHO PQ'd/ ERP reviewed and locally approved products.
- The volumes procured for SOF/DCV FDC were too small to determine a representative pricing trend.
- In-country prices mentioned are public sector prices paid by the government in each country, if available, or the lowest identified private sector price if a public sector price is not available.
- **Cambodia**: Following the end of Médecins Sans Frontières' engagement in Cambodia in December 2021, as of the report publication date, Cambodia is not procuring DAAs for a public sector program. Prices reflect those of commodities (SOF/DCV FDC, RDT, VL) procured by the co-infection program via in-country GFATM procurement mechanisms and are paid for through GFATM under this program; Price for SOF/VEL FDC is from 2020.
- **India**: Prices mentioned are from the previous market report.
- **Indonesia**: DCV 60 from Natco (US$13) and Hetero (US$12) are both available on the e-Katalog. Price from Hetero is reflected in the graph.
- **Myanmar**: The price indicated in the in-country DAA price graph is for SOF+DCV; Prices of SOF & DCV individually are unavailable; Prices for DAAs and VL are from 2019.
- **Vietnam**:
  1. HCV RDT and HCV VL prices in Vietnam are taken from 2021 Health Insurance data which reflects the aggregate price accessed by each province where services are being provided and reimbursed by health insurance. A certain percentage of this cost (approximately 80%) is reimbursed by health insurance.
  2. In Vietnam, procurement of commodities is coordinated individually by provinces and health facilities. DAA prices for Vietnam reflect the lowest bidding prices from health facilities as of December 2021. These bidding prices act as a ceiling price; in reality, facilities might be accessing commodities at a lower price.
  3. Vietnam's national HIV/HCV co-infection program, led by the Vietnam Administration for HIV/AIDS Control and supported financially by the GFATM, procured 12 weeks of SOF/DCV at US$100. As the program is slated to end in August 2022, we have not reflected this price.

Acknowledgments:

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