

FORGING A PATH TO HCV ELIMINATION: SIMPLER TESTS AND AFFORDABLE GENERICS

Report of the World Community Advisory Board
on HCV Generics and Diagnostics
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MEETING ORGANIZERS



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LIST OF ABBREVIATIONS

API	Active Pharmaceutical Ingredient	MdM	Médecins du monde
APN+	Asia-Pacific Network of People Living with HIV/AIDS	MENA	Middle East and North Africa
BMS	Bristol-Meyers Squibb	MIC	Middle-Income Country
CAB	Community Advisory Board	MoH	Ministry of Health
cAg	Core Antigen	MPP	Medicines Patent Pool
CHAI	Clinton Health Access Initiative	MSF	Médecins Sans Frontières
CE	Conformité Européene certification	PEPFAR	U.S. President's Emergency Plan for AIDS Relief
CL	Compulsory License	PLWHCV	People Living with Hepatitis C Virus
DAA	Direct Acting Antiviral	PLWHIV	People Living with Human Immunodeficiency Virus
DCV	Daclatasvir	PoC	Point-of-Care Test
DNDi	Drugs for Neglected Diseases Initiative	RBV	Ribavirin
FIND	Foundation for Innovative New Diagnostics	RDT	Rapid Diagnostic Test
HBDC	High Burden Developing Country	RVD	Ravidasvir
HCV	Hepatitis C Virus	SOF	Sofosbuvir
HIC	High-Income Country	SVR	Sustained Virological Response
HIV/AIDS	Human Immunodeficiency Virus/ Acquired Immunodeficiency Syndrome	TAG	Treatment action group
HPV	Human Papillomavirus Virus	TB	Tuberculosis
I-MAK	Initiative for Medicines, Access and Knowledge	USAID	United States Agency for International Development
IP	Intellectual Property	VEL	Velpatasvir
ITPC	International Treatment Preparedness Coalition	VL	Voluntary License
LED	Ledipasvir	WHO	World Health Organization
LMIC	Low- and Middle-Income Country	WHO PQ	World Health Organization Pre-Qualification

EXECUTIVE SUMMARY

Over the past several years, there has been a substantial expansion of community engagement on the hepatitis C Virus (HCV). Communities—along with allies in civil society—have played a key role in the acceleration of government responses to HCV. Many of the organizations involved in HCV advocacy have long worked on HIV issues, translating many lessons learned from the fight against AIDS. Such activism provides a blueprint for the international response to HCV.

Significant barriers—such as financing, awareness, complicated and unaffordable diagnostics, centralized service delivery, and stigma—obstruct the sustainable scaling up of prevention, testing, and treatment services. Despite the recent emergence of a cure in 2014, it is estimated that annual new infections continue to outpace the annual number treated.¹

High prices for direct acting antivirals (DAAs) in high-income countries (HICs) have dominated the discourse and made hepatitis C treatment the prime example for a broken drug development system. These high prices have impacted prices in upper middle-income countries, leading to treatment rationing. Such high prices are all-the-more unacceptable when feasible generic prices are taken into account. In less than two years, a 12-week treatment course has become available for less than US\$ 150 when procured under robust generic competition.

Yet, as shown in countries with low-cost generics, high prices are not the only bottleneck blocking progress towards HCV elimination. Improved awareness is desperately needed. Stigma towards key populations—including people who use drugs, prisoners, men who have sex with men, and some indigenous communities—is also a significant barrier. Beyond these barriers, diagnostics are expensive and poorly adapted to decentralized settings. The fact that testing costs must often be paid out-of-pocket exacerbates access limita-

tions. Finally, limited financing for the HCV response remains a key barrier; in fact, the nearly exclusive dependence of HCV programs on domestic financing sources is a key difference between the present global response to HIV and HCV.

To address the need for strengthened advocacy on affordable tests and generic treatment, the HCV Community Advisory Board brought together 37 treatment activists from 17 countries to meet with representatives from three generics and three diagnostics companies. The meeting was an opportunity for activists to present demands and obtain strategic information from companies on critical access issues relating to pricing policies, registration, and procurement, with particular focus on low- and middle-income countries.

In the meetings with generic companies, the CAB discussed treatment access barriers and expressed our demands. The meetings with diagnostics companies revealed—in addition to the importance of price-related barriers for serology and viremia testing—the need to develop advocacy tools and trainings on HCV diagnostics.

In discussions on access to both diagnostics and medicines, there were several common themes. It was noted that distributor markups and customs fees are creating further price barriers that further strain limited budgets. Reinforcing dynamics—the need for scaled up diagnostics to drive treatment volumes and treatment regimens that can treat all sub-types of HCV—were also emphasized.

The World CAB recognized the litany of challenges before us, highlighting the need for: expansion of options for diagnostics technologies and integration with existing multi-disease platforms; simplification of diagnostic algorithms; simplification of treatment protocols; reduction of prices on diagnostics and medicines; reduction of add-on fees from customs and distributors; reduction of regulatory bottlenecks; elimination of intellectual property (IP) barriers; greater domestic and international financing. While the meeting took stock of these barriers, the World CAB also illustrated the solidarity that will be so crucial to overcoming existing obstacles.

November 2017

1. World Hepatitis Organization. *Global Hepatitis Report*. Geneva: World Hepatitis Organization; 2017 April.

HEPATITIS C



FREE THE CURE

INTRODUCTION

ABOUT THE HCV WORLD CAB

Community Advisory Boards have long played an important role in the push to expand access to medicines and in the formulation of demands for improved responses to public health challenges. HCV Community Advisory Boards have borrowed from the precedent established by HIV activists. One key example was the 2004 HIV World Community Advisory Board formed by the International Treatment Preparedness Coalition, which was comprised of people living with HIV/AIDS and fellow comrades. CAB meetings at national, regional, and global levels have played a critical role in the exchange of information and the formulation of specific treatment access demands aimed at originator (patent holding) drug companies, scientists, and government representatives.

In this tradition, the HCV World CAB is underpinned by human rights principles. Beyond the right to health and its subsequent implications for universal access to medicines, the emphasis on human rights seeks to highlight that universal rights apply equally to key populations, many of whom suffer from active discrimination and are denied equitable access to services. CABs recognize that the most-affected communities—in particular people who inject or use drugs—play an essential role in the advocacy required to improve policies at the national and international levels. Since 2014, there have now been three different iterations of the HCV World CAB to provide space for activists in low- and middle-income countries (LMICs) to discuss some of the most pressing concerns on HCV treatment access. This iteration is the first to directly integrate diagnostic companies into the agenda.

The following report will first highlight developments in the HCV landscape, then provide an overview of the key takeaways from the exchange with generic and diagnostic companies.

EVOLUTION SINCE THE PREVIOUS WORLD CAB

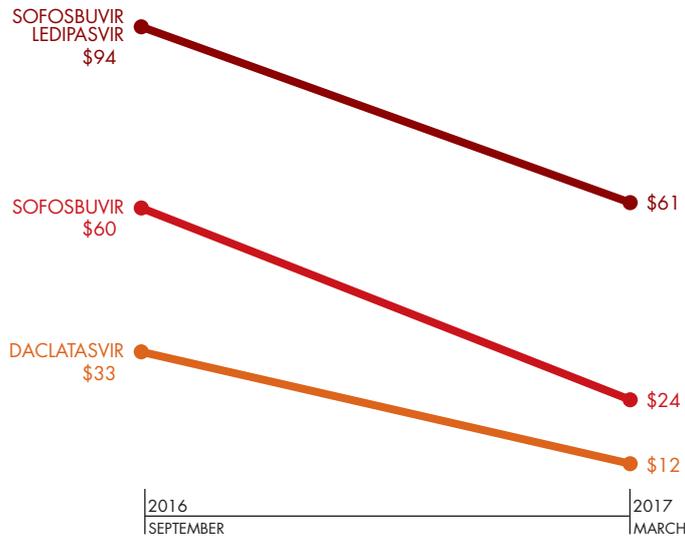
Since previous iterations of the HCV World CAB², the HCV landscape has witnessed significant changes. When community members met in February 2014, sofosbuvir—the backbone of the most widely-accessed treatments for HCV—had only just entered the US market a few months prior (December 2013). Generic versions for DAAs did not yet exist, and the World Health Organization (WHO) Global Strategy on Viral Hepatitis had not yet been approved (May 2016). Highly effective multi-drug combinations based on sofosbuvir and other DAAs followed, including regimes capable of treating all six HCV genotypes, known as pangenotypic treatments (June 2016).^{3 4} The eye-popping price tags in high-income countries dominated the discourse and fueled concern that prices would generate significant barriers to country-level HCV responses in LMICs. For many countries, these fears have proven justified, with barriers extending to most HICs as well. From Brazil to the UK, prices have led to treatment rationing. In other countries facing monopolies, rationing is an afterthought, as high prices have essentially stalled the implementation of DAA treatment scale-up.

The impact of these artificial barriers are brought into focus by the fact that, while pricing fears in monopoly markets have proven justified, pricing hopes for generic markets have been widely vindicated. Just under two years after generics of DAAs first appeared, a full 12-week treatment is available for under US\$ 150 when procured under robust generic competition. In turn, the emergence of affordable generics has played a key role in spurring ambitious responses to HCV at the national level. Alternatively, the absence of affordable generics continues to present a key bottleneck in middle-income countries; simple budget impact calculations demonstrate that while low-priced generics alone may not be sufficient to achieve elimination, affordable treatment is a necessity for any sustainable scale-up.

It has become increasingly clear that addressing interrelated challenges of financing, awareness, diagnostics, and service delivery is fundamental to the successful implementation of any scale-up. These challenges have come into particular focus in those areas where low-price generics are available.

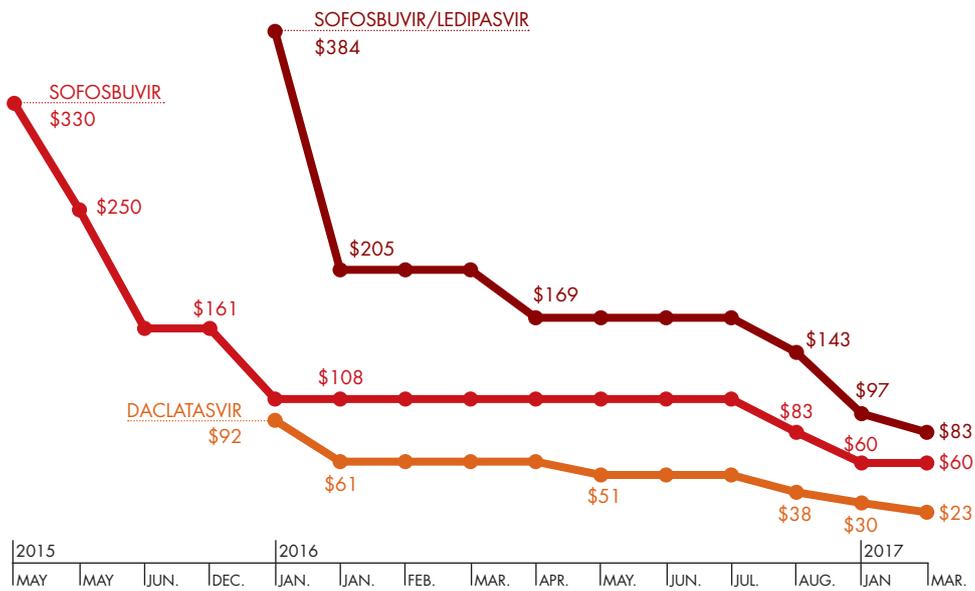
2. *Pills Cost Pennies, Greed Costs Lives - 1st Hepatitis C Virus World Community Advisory Board Report*. July 2014. <http://hepcoalition.org/advocate/advocacy-tools/article/1st-hepatitis-c-virus-world?lang=en>
 3. Treatment Action Group (TAG). *Pipeline Report*; July 2015. <http://www.pipelinerreport.org/2015/hcv>.
 4. TAG. *Pipeline Report*; July 2017. <http://www.pipelinerreport.org/2017/hcvdaas>.

FIGURE 1 PRICE PER BOTTLE* OF INDIAN GENERIC DAAs IN PUBLIC SECTOR



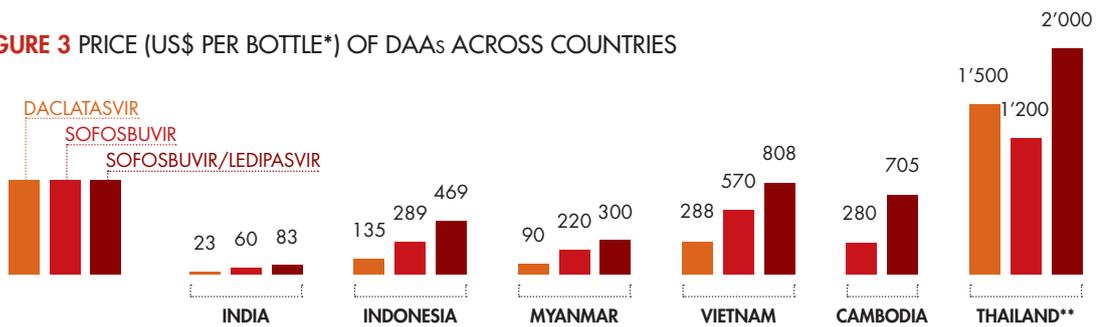
Source: TREAT Asia/amfAR, Bangkok, Thailand. July 2017

FIGURE 2 PRICE PER BOTTLE* OF INDIAN GENERIC DAAs IN PRIVATE SECTOR



Source: TREAT Asia/amfAR, Bangkok, Thailand. July 2017

FIGURE 3 PRICE (US\$ PER BOTTLE*) OF DAAs ACROSS COUNTRIES



Source: MSF and TREAT Asia/amfAR, Bangkok, Thailand. July 2017

* One bottle contains 28 pills. For a 12-week treatment with a given DAAs, three bottles are required

** Thailand has been included to Gilead HCV voluntary license and have now access to generic SOF, SOF/LDV and SOF/VEL

MEETING PART ONE: ACTIVIST WORKSHOP

The first day of the World CAB consisted of a community workshop which delved into treatment access issues, which was attended by community members only. This helped strengthen relationships among activists and allowed sharing of strategic information in confidence. It framed the context of current efforts to eliminate HCV and reflected on some of the lessons learned from previous CABs, both in HIV and HCV. Information on the latest DAAs, diagnostics, barriers to access, and notable advocacy initiatives to respond to the epidemic were shared and discussed.

UPDATE ON GLOBAL HCV CONTEXT

An estimated 71 million people are living with HCV around the world. Extrapolating from WHO estimates, 1 person dies every 80 seconds as a result of HCV.⁵ Worldwide, HCV is responsible for nearly 400,000 deaths annually. The burden is felt most in low- and middle-income countries, where two-thirds of people living with HCV reside.

The HCV epidemic disproportionately impacts key populations, with particularly high prevalence rates among people who inject drugs. It is estimated that at least ten million people who inject drugs have been infected by HCV,⁶ and that approximately 2.3 million people are co-infected with HCV and HIV.

In 2014, the WHO published HCV prevention, treatment and care guidelines (revised in 2016). At the

World Health Assembly in May 2016, member states approved a global strategy for elimination of viral hepatitis as a public health concern by 2030. Specifically, the WHO targets call for 90% reduction in HCV incidence and 65% reduction in HCV related mortality by 2030. These reductions will be achieved through diagnosis of 90% of individuals living with chronic hepatitis C infection, and treatment of 80% of those individuals diagnosed. To achieve the targets, modeling studies suggest that 5-10% of people diagnosed with HCV must be treated each year.⁷

At present, ballpark estimates suggest that—at the global level—annual new infections still outnumber annual treatments.⁸ Though the gap is closing, these estimates are a sobering reminder of the challenge that lies before us and the urgency of building on existing momentum to address hepatitis C.

PRICING AND GENERIC COMPETITION

List prices of DAAs (before rebates or patient assistance programs) in many high-income countries range between US\$ 54,600 to US\$ 83,319 for a 12-week course.⁹ These prices are orders of magnitude higher than generic production costs, estimated to be below US\$ 76 per treatment course.¹⁰

When generic competition enters the market, prices can drop dramatically, with DAAs providing classic examples of the impact of generic competition. For instance, in two years the price of a bottle of sofosbuvir/ledipasvir (SOF/LED) has reduced from US\$ 384 to US\$ 83 in India's private sector. The proliferation of generics, combined with procurement at scale, has seen public sector prices fall in just six months to US\$ 108¹¹ for a 12-week treatment. In other words, generic competition has cut the price to less than 0.1% of the initial price demanded by the originator companies.

However, pricing for identical DAAs can vary widely between countries in the same region and with similar income levels (Figure 3). For example, while generic sofosbuvir/ledipasvir in the Punjab public health sector costs US\$ 61 per bottle, patients in Vietnam pay US\$ 800 per bottle, which is about 40% of the per capita income (US\$ 2,050 in 2016, purchasing power parity).¹²

These price variations reveal disparities in access, gaps and delays in registration under voluntary licenses, and imbalances in negotiating power for affordable drug

5. WHO. *Global Hepatitis Report*. Geneva: WHO; 2017 April.

6. Nelson PK, Mathers BM, Cowie B, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. *Lancet* 2011; 378: 571–83.

7. *Ibid.*

8. WHO. *Global Hepatitis Report*. Geneva: WHO; 2017 April.

9. Médecins du Monde and Treatment Action Group. Dying at these prices: Generic HCV cure denied. mapCrowd Report 2; 2016 July. http://mapcrowd.org/public/pdf/EN_mapCrowd_Report2.pdf (Accessed 2017 September 28).

10. Technology and Market Landscape, HCV Medicines. UNITAID, August 2017. Citing Andrew Hill. https://unitaid.eu/assets/HCV-Medicines-Landscape_Aug-2017.pdf

11. Reported at SEARO Viral Hepatitis Meeting, April 2017. Price refers to Punjab public procurement tender for 12-weeks of SOF-DCV.

12. World Bank. International Comparison Program database. Accessed 2017 September 16.

TABLE 1 REGISTRATION OF ORIGINATOR SOFOSBUVIR, SOFOSBUVIR/LEDIPASVIR AND SOFOSBUVIR/VELPATASVIR

	APPROVED			FILED		
SOF	Argentina Cameroon Dominican Rep. El Salvador Indonesia Nigeria Philippines Thailand Uruguay	Bolivia Chile Ecuador India Mexico Pakistan Rwanda Tunisia Uzbekistan	Brazil Colombia Egypt Georgia Mongolia Peru Tanzania Ukraine Venezuela	Kenya Vietnam	South Africa	Uganda
SOF/LDV	Argentina Chile Egypt Georgia Mauritius Morocco Rwanda Tunisia	Bolivia Costa Rica El Salvador India Mexico Peru Tanzania Ukraine	Cameroon Dominican Rep. Ethiopia Kyrgyzstan Mongolia Philippines Thailand Uruguay	Brazil Guatemala Nigeria South Africa	Colombia Indonesia Pakistan Uganda	Ecuador Kenya Panama Venezuela
SOF/VEL	Argentina	Georgia	Mexico	Brazil Costa Rica Pakistan South Africa	Chile Dominican Rep. Panama Thailand	Colombia India Philippines

Source: Gilead. July 2017.

TABLE 2 APPROVAL AND FILING OF GENERIC DAAs

	APPROVED			FILED		
SOF	Azerbaijan Cameroon El Salvador Guatemala Kazakhstan Malawi Morocco Nepal Saudi Arabia Turkeministan	Bhutan Chad Ethiopia India Kyrgystan Moldova Mozambique Nicaragua Sri Lanka Ukraine	Cambodia Congo Republic Gabon Indonesia Lebanon Mongolia Myanmar Rep. Côte d'Ivoire Sudan Uzbekistan	Belarus Botswana Guyana Jordan Madagascar Namibia Pakistan Senegal Tajikistan Tunisia Zambia	Benin Burkina Faso Honduras Kenya Mali Nicaragua Philippines Sierra Leone Tanzania Uganda Zimbabwe	Bolivia Ghana Indonesia Liberia Morocco Nigeria Rwanda South Africa Togo Vietnam
SOF/LDV	Cambodia Gabon Mongolia Turkmenistan	Chad India Myanmar Uzbekistan	El Salvador Kyrgystan Rep. Côte d'Ivoire	Burkina Faso Congo Liberia Mozambique Sri Lanka	Burundi Guatemala Malawi Nicaragua Tajikistan	Cameroon Honduras Mali Senegal Zambia
SOF/VEL	Cambodia	Nepal		Myanmar	India	
DCV	Cambodia India Morocco Turkeministan	Chad Indonesia Myanmar Uzbekistan	Gabon Kyrgyzstan Nepal	Benin Cameroon El Salvador Liberia Mongolia Senegal Tog	Burkina Faso Congo Republic Guatemala Mali Mozambique Sri Lanka Vietnam	Bolivia Costa Rica Honduras Madagascar Nicaragua Tajikistan

Source: TREAT Asia/amfAR, Pharco. July 2017

prices, particularly for countries with smaller patient populations deemed unprofitable. In addition, originator patent monopolies enforced through international trade agreements and lack of competition between generics manufacturers can inflate prices. Within countries, markups by middle agents such as local distributors, pharmacies and hospitals also limit affordability. In fact, one may argue that robust generic DAA competition exists in only a handful of countries.

REGISTRATION GAP

The lack of registration of DAAs in dozens of LMICs reflects a diverse array of structural obstacles such as local clinical trial requirements, limited patient population size, lack of fast-track channels, and under-resourced regulatory agencies.

Within the territories covered by voluntary licenses with originator companies, it is important to note that IP barriers are half the battle to obtaining a legal path for generic competition: regulatory approval and competition among at least three generic manufacturers are a key complementary step. In this context, registration by the patent holding originator company is often key to timely regulatory approval in LMICs and a key step toward facilitating the entry of generic competition. Therefore, we need companies that have established voluntary licenses to be proactive in their registration and responsive to the regulatory follow up of licensees.

As of July 2017, sofosbuvir has been approved in approximately 50 low- and middle-income countries. However, as of July 2017, less than ten LMICs had approved the DAAs facilitating pangenotypic treatment (SOF/DCV or SOF/LED). So while nearly half of LMICs continue to face regulatory barriers to DAA treatment scale-up, over 90% of LMICs currently face regulatory barriers to scale-up of pangenotypic regimens. Due to the key role that pangenotypic regimens can play in the simplification of diagnostic protocols (i.e. through elimination of the logistically and financially burdensome step of genotyping tests), accelerated registration will play a key role in the ability for countries to mount effective HCV responses. Furthermore, it is important to emphasize that generic competition plays

an instrumental role in price reductions; such competition requires that multiple generics are registered.

In many cases, accelerated registration of generic formulations will be facilitated by: registration of the formulation by the originator, and submission/approval of the generic formulation by the WHO Prequalification program (WHO-PQ). Five companies (Mylan, Cipla, Hetero, Pharco, and Strides) have applied for WHO pre-qualification of sofosbuvir. As of October 2017, Mylan and Cipla have received pre-qualification.

INTELLECTUAL PROPERTY BARRIERS

HCV treatment activists have drawn many lessons from the HIV community's hard-won, successful efforts to expand access to generic ARVs through challenges to big Pharma monopolies. Such experiences are relevant to HCV activists for the simple reason that pharmaceutical companies have employed similar strategies in rolling out medicines for both diseases. Notably, in issuing voluntary licenses (VLs) and proclaiming their commitment to access, originator companies have consistently excluded middle-income countries from voluntary licenses.¹³

There are three voluntary licensing agreements concerning HCV DAAs.

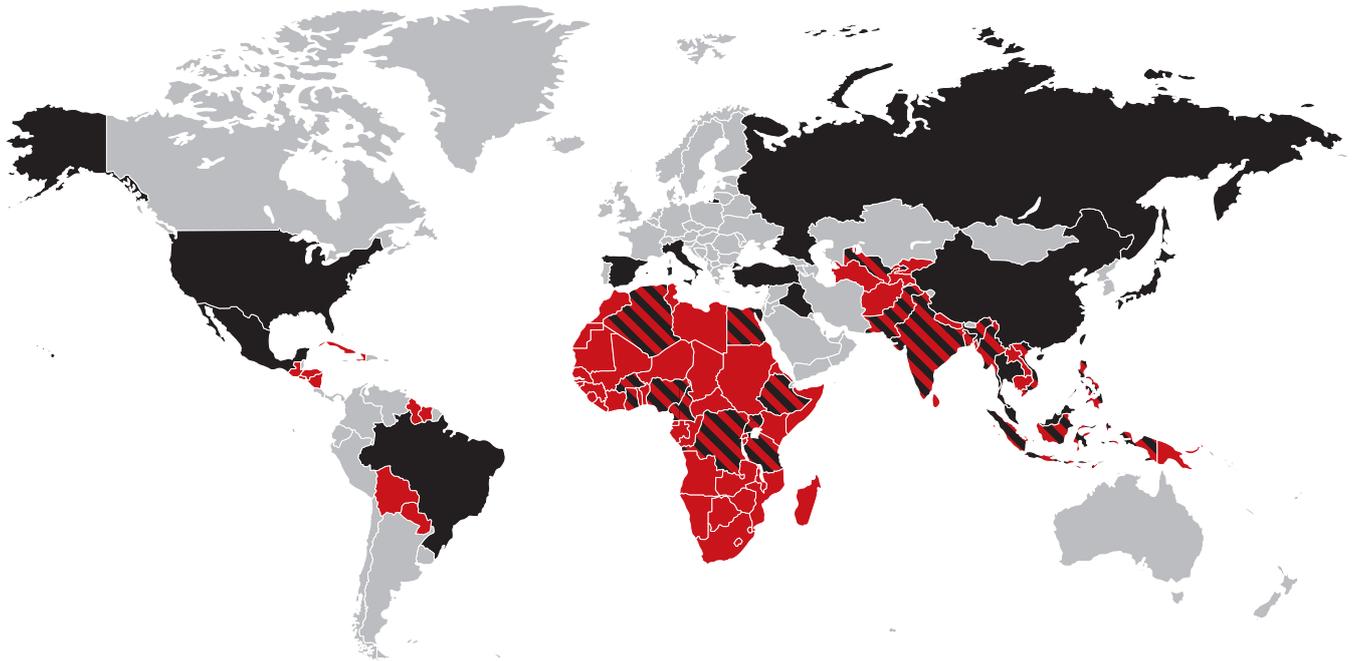
Gilead: As of September 2017, Gilead Sciences has granted licenses to generic companies to market sofosbuvir, sofosbuvir/ledipasvir and sofosbuvir/velpatasvir (SOF/VEL) in 105 low income and selected middle income countries. The voluntary licenses require a 7% royalty to be paid to Gilead on sales of sofosbuvir or sofosbuvir-based combinations. Several dozen upper middle-income countries have been left out of the license (see table below). Gilead has expanded the license twice, adding ten countries in August 2015 and four countries in August 2017. Although 11 Indian generic companies have signed the licensing agreement, only three (Mylan, Hetero and Natco) are currently producing drugs under the license.

Bristol-Myers Squibb: In 2016, Bristol Myers-Squibb granted the Medicines Patent Pool a license for daclatasvir (DCV), allowing the marketing of generic formulations in 112 LMICs. Seven Indian generic companies have signed the licensing agreement.

Presidio: Presidio granted DNDi a non-exclusive voluntary license for the NS5A-inhibitor ravidasvir; as

13. *Pills Cost Pennies, Greed Costs Lives - 1st Hepatitis C Virus World Community Advisory Board Report*. July 2014. <http://hepcoalition.org/advocate/advocacy-tools/article/1st-hepatitis-c-virus-world?lang=en>

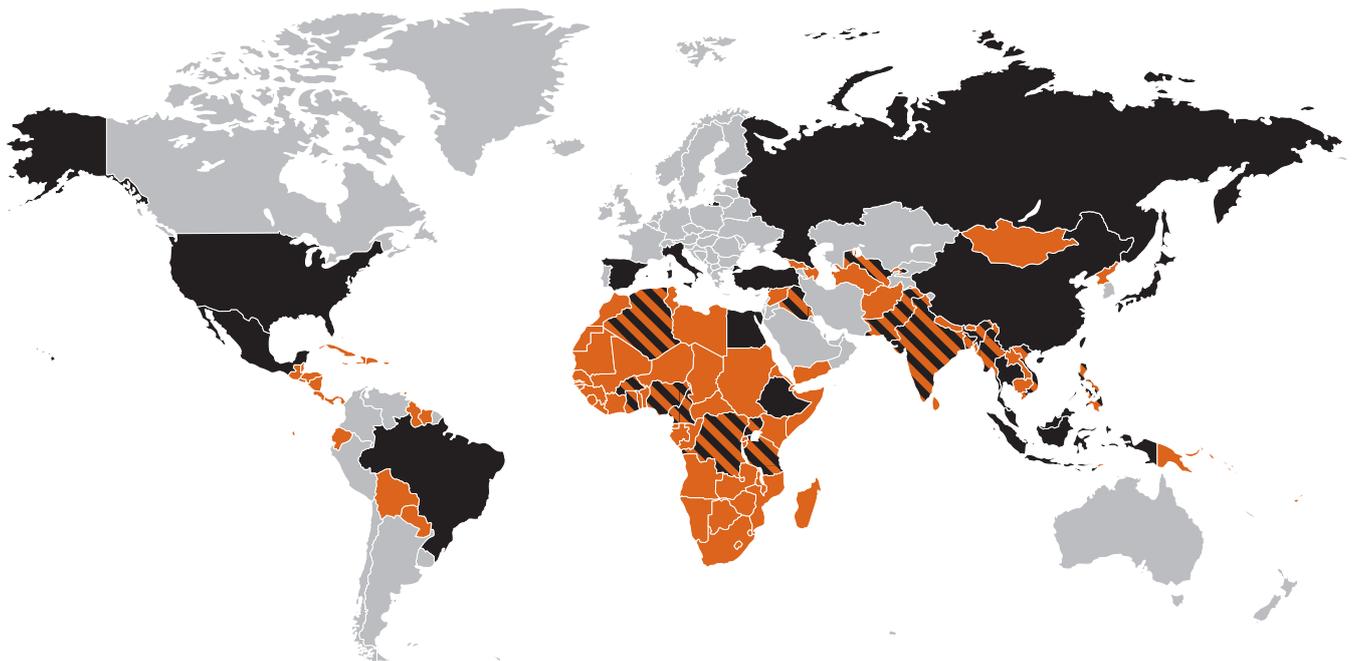
MAP 1 COUNTRIES INCLUDED IN THE GILEAD VOLUNTARY LICENSE



Countries with more than 500,000 HCV cases.
 Countries included in the Gilead voluntary license.
 Countries with more than 500,000 HCV cases included in the Gilead voluntary license.

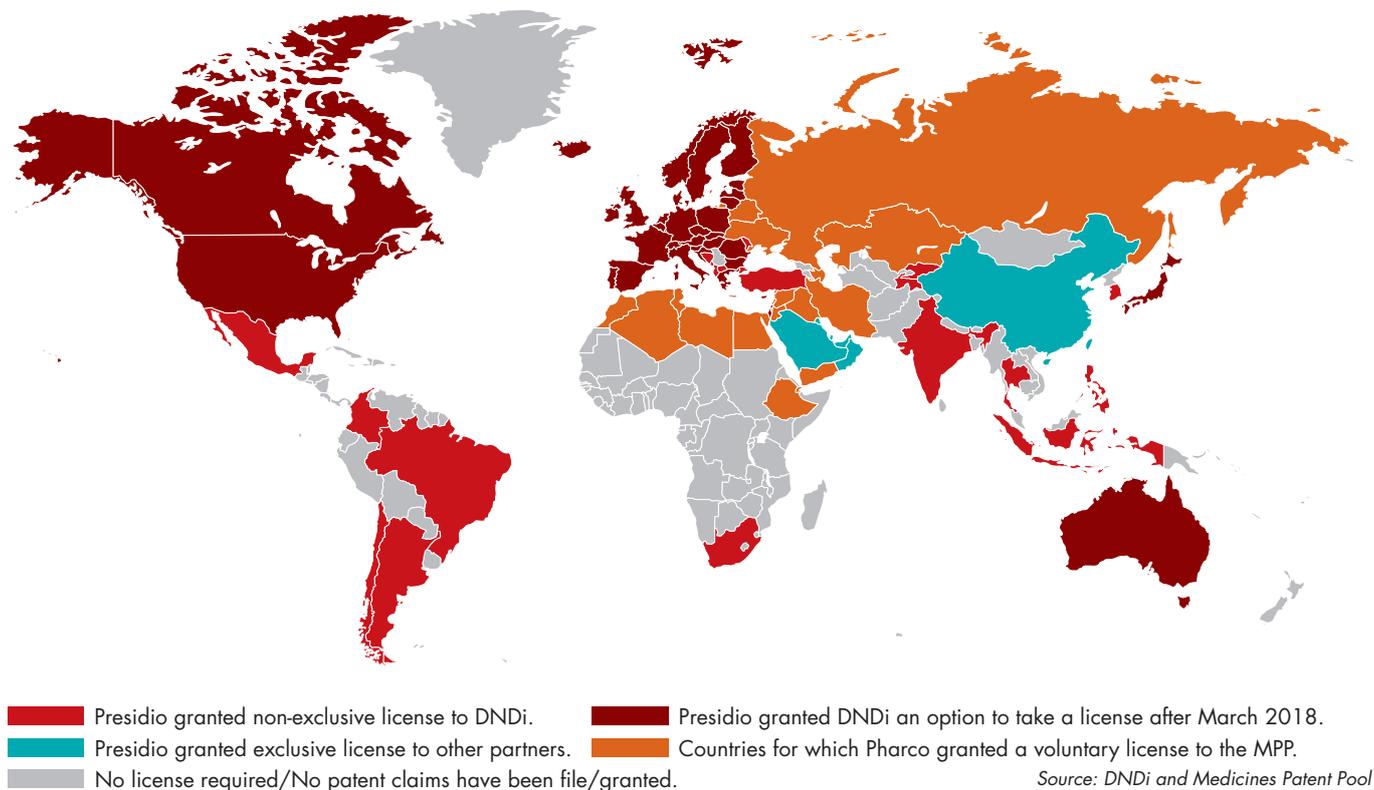
Source: Gilead

MAP 2 COUNTRIES INCLUDED IN THE BMS/MPP VOLUNTARY LICENSE



Countries with more than 500,000 HCV cases.
 Countries included in the BMS/MPP voluntary license.
 Countries with more than 500,000 HCV cases included in the BMS/MPP voluntary license.

Source: Medicines Patent Pool

MAP 3 COUNTRIES INCLUDED IN THE PRESIDIO/DNDI AND PHARCO/MPP VOLUNTARY LICENSES

a result, the Americas and Europe will both have access to generic formulations of a critical complement to sofosbuvir. The generic company Pharco (Egypt) has agreed to supply DNDi with the combination sofosbuvir plus ravidasvir for its clinical studies for US\$ 300 per course of treatment. For the scale-up of this regimen, if approved, Pharco has agreed to set the commercial price at US\$ 294 or less per treatment course. Studies are ongoing to confirm the regimen's promising pangenotypic potential.¹⁴

In middle- and high-income countries excluded from the voluntary licenses, exorbitant monopoly-enabled prices have strained health budgets.

As a result, many of the richest countries in the world have imposed treatment restrictions; such treatment rationing has triggered significant criticism of the pharmaceutical industry and raised public awareness of

high drug prices. The enormous costs imposed on public treasuries and health systems led to an investigation by the US Senate. Senator Wyden summarized its findings by stating, "Gilead pursued a calculated scheme for pricing and marketing its [h]epatitis C drug based on one primary goal, maximizing revenue, regardless of the human consequences. There was no concrete evidence in emails, meeting minutes or presentations that basic financial matters such as R&D costs or the multi-billion dollar acquisition of Pharmasset, the drug's first developer, factored into how Gilead set the price."

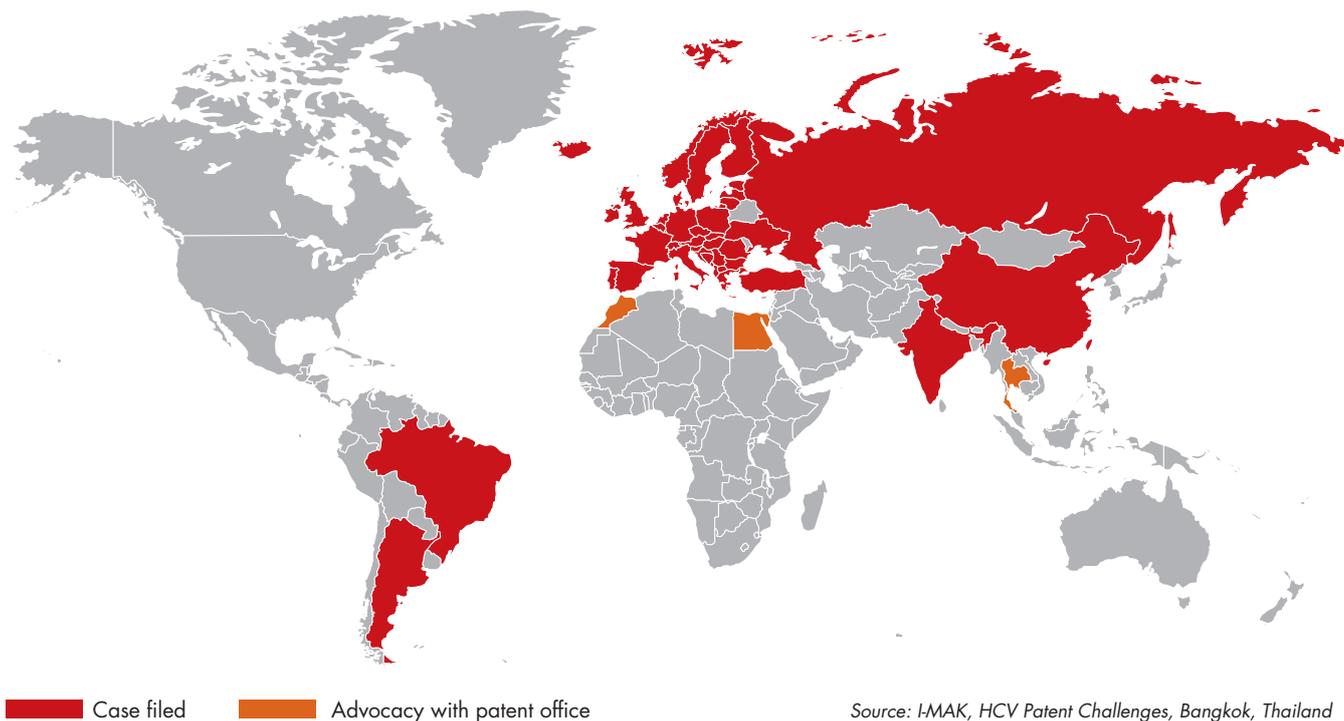
Following the successful precedent established by fellow HIV activists, many in civil society have advocated that governments issue compulsory licenses, which permit production or importation of generic version of a patented drug without the consent of the patent holder¹⁵. In several countries, there have been discussions concerning the possibility of issuing compulsory licenses on HCV drugs. In some countries, serious exploration of compulsory licensing has influenced price negotiations and ultimately contributed to significant discounts. In the United States, the Louisiana Health Secretary has proposed using U.S. Code Section 1498, a federal law that could appropriate the patent and contract with a generic supplier to produce sofosbuvir and sofosbuvir/ledipasvir at lower prices¹⁶.

In September 2017, Malaysia became the first country to issue a compulsory use license for a DAA —sofosbuvir

14. Press Release. Medicines Patent Pool. "The Medicines Patent Pool and Pharco Pharmaceuticals Sign License for Promising Hepatitis C Drug Candidate Ravidasvir." 21 April 2017. (Accessed October 2017) <https://medicinespatentpool.org/mpp-media-post/the-medicines-patent-pool-and-pharco-pharmaceuticals-sign-licence-for-promising-hepatitis-c-drug-candidate-ravidasvir/>

15. *Pills Cost Pennies, Greed Costs Lives - 1st Hepatitis C Virus World Community Advisory Board Report*. July 2014. <http://hepcoalition.org/advocate/advocacy-tools/article/1st-hepatitis-c-virus-world?lang=en>

16. Tribble SJ. "Louisiana proposes tapping a century-old patent law to cut hepatitis C drug prices," *Washington Post*. 2017 May 2.

MAP 4 HCV PATENT CHALLENGES ACROSS THE WORLD**TABLE 3** STATUS OF HCV PATENT OPPOSITIONS CASES FILED BY CIVIL SOCIETY

PATENT OPPOSED	PATENT INTERNATIONAL PUBLICATION NUMBER	COUNTRY	OPPONENT (CIVIL SOCIETY ONLY)	YEAR	CHALLENGE STATUS
SOFOBUVIR (PRODRUG)	WO2008121634	India	DNP+, I-MAK	2013	Under examination.
		Europe*	MDM	2015	Maintained in an amended form; under appeal.
		Argentina	FGEP	2015	Under examination.
		China	I-MAK	2015	Rejected, In 2017 rejection upheld over Gilead's appeal.
		Russia	ITPCru	2015	Partially revoked (Appeal).
		Thailand	AAF	2016	Under examination.
SOFOBUVIR (BASE COMPOUND/MOLECULE)	WO2005003147	India	DNP+, I-MAK	2013	Refused first but granted later. In the process of appeal.
		Europe*	MDM	2017	Under examination.
		Europe*	MSF	2017	Under examination.
		Europe*	Consortium of six European NGOs	2017	Under examination.
		China	I-MAK	2017	Invalidation filed, case pending.
		Argentina	FGEP	2017	Opposition filed.
		Brazil	ABIA	2015	Opposition filed, preliminary rejection by ANVISA, under examination.
SOFOBUVIR (POLYMORPHS)	WO2011123645	India	DNP+, I-MAK	2017	Under examination.
		Ukraine	AUN of PLWH, I-MAK	2015	Under examination.
SOFOBUVIR (PROCESS)	WO2012012465	Ukraine	AUN of PLWH	2016	Rejected.
SOFOBUVIR/LEDIPASVIR (COMPOUND)	WO2013040492 A2	Ukraine	AUN of PLWH	2016	Under examination.
DACLATASVIR (CRYSTALLINE)	WO2009020828	India	DNP+, I-MAK	2017	Under examination.
DACLATASVIR (INTERMEDIATE)	WO2008021927	India	LC	2017	Under examination.
VELPATASVIR (Base)	WO2013075029	India	DNP+, I-MAK	2017	Under examination.

— thereby enabling the procurement of an affordable generic version by the national health program¹⁷. As demonstrated in the Malaysian case, local activism and international solidarity for these interventions are powerful contributions to expand treatment access¹⁸.

Another strategy to overcome IP barriers that has proven successful is to challenge patents in order to ensure that patent offices subject applications to the full rigor of a country's intellectual property law¹⁹. Since the first World CAB, a growing number of patent opposition cases have been filed by civil society. Oppositions have been filed in: Argentina, Brazil, China, India, Russia, Ukraine, and the European Union. While most oppositions have targeted the primary patents for sofosbuvir, patents covering daclatasvir and velpatasvir have also been opposed. The challenges have led to several rejections and partial or full patent revocations (see Table 3).

HCV DIAGNOSTICS: BACKGROUND AND BARRIERS

In the past fifteen years, significant resources have been dedicated to the HIV response in LMICs. As a result, nearly 70% of people living with HIV are estimated to be aware of their status (WHO 2016). Similar estimates for people living with HCV are less robust; in many if not most LMICs, the percentage of individuals aware of their status falls below 5%. The path to similar coverage of HCV diagnosis will require a significant increase in political and financial commitments. It will also require technological innovations that deliver affordable tests that may be adapted at

scale by health care workers in decentralized settings. Although HCV may take many lessons from efforts to strengthen the HIV continuum-of-care, HCV diagnosis is a two step process requiring HCV specific interventions. While HIV can be diagnosed with a single rapid antibody test, HCV requires an RNA test to confirm chronic HCV infection, making diagnosis more costly and time consuming.

Individuals and health care workers are not sufficiently aware of HCV risks and HCV treatment, and few health systems cover viral load²⁰ tests through public insurance. In many places, HCV viral load tests are roughly double the costs of HIV viral load, and in the private sector, HCV viral loads are frequently nearly twice as costly as public sector HCV viral loads. Genotyping tests to determine the specific HCV subtype are particularly expensive, typically representing the most costly step of the diagnostic process.

These high prices are exacerbated by the fact that, as mentioned above, many individuals must finance the tests out-of-pocket. With the availability of high quality generics, HCV diagnostics need to catch up. Greater access to diagnostics will prove key to generating the volume of procurement necessary to maximize generic price reductions. The simplification of diagnostic protocols will be key to generating such a virtuous cycle. In turn, a catalyst for the simplification of protocols is the availability of affordable pangenotypic regimens.

At present, a very general overview of the diagnostic protocol involves: screening with an anti-HCV antibody test²¹ is followed by confirmation of an active infection with an HCV RNA viral load qualitative and/or quantitative test, or with an HCV core antigen test (cAg)²². Following confirmation, a liver disease staging and genotyping (when pangenotypic treatment is not available). Of course, there are various iterations of the protocol.

Due to the interrelated, complex variables found across national health systems and service delivery at the community level, optimal screening and testing pathways will remain highly specific to local contexts. At present, most health systems rely on a highly-centralized process for confirmation of HCV viremia.

In order to frame and organize key parameters for comparison, participants reviewed the characteristics of an ideal point of care (PoC) rapid diagnostic test (RDT) in decentralized settings, a profile that highlighted a product that could diagnose active HCV viremic

17. For more information: <http://hepcoalition.org/news/press-releases/article/apn-joins-mtaag-in-congratulating-malaysia-on-sofosbuvir-compulsory-license>

18. *Pills Cost Pennies, Greed Costs Lives - 1st Hepatitis C Virus World Community Advisory Board Report*. July 2014. <http://hepcoalition.org/advocate/advocacy-tools/article/1st-hepatitis-c-virus-world?lang=en>

19. *Pills Cost Pennies, Greed Costs Lives - 1st Hepatitis C Virus World Community Advisory Board Report*. July 2014. <http://hepcoalition.org/advocate/advocacy-tools/article/1st-hepatitis-c-virus-world?lang=en>

20. Viral load refers to a diagnostic test that confirms active infection by detecting the presence of virus in blood. A qualitative test simply confirms virus is present in the sample. A quantitative test counts how many copies of the virus are found in a specified amount.

21. Anti-HCV antibody test is the initial HCV screening test that detects exposure to the hepatitis C virus. It does not confirm active infection. Blood or saliva can be used for antibody tests.

22. Hepatitis C Virus Core Antigen testing confirms HCV infection by detecting specific viral proteins (antigens) in the blood which are released into plasma during the reproduction of the virus and can be detected from early on and throughout the course of infection. Core antigen can be detected two weeks after infection.

infection, provide baseline assessment, allow same-day diagnosis and treatment initiation, and confirm post-treatment cure.

Presently, there are two point-of-care rapid diagnostic HCV antibody tests in the field that have been approved as reliable by regulatory authorities (WHO PQ, Conformité Européenne [CE] marked): Oraquick by Orasure Technologies and SD Bioline by Alere.

The Oraquick test from Orasure Technologies provides results via capillary blood (finger stick) and oral saliva swab. The discounted price negotiated for one medical NGO is €7 per test, which remains beyond the limits for most LMICs with high disease burdens.²³

The World CAB met with Alere, producer of the other pre-qualified antibody test, known as SD Bioline. Alere manufactures SD Bioline at two facilities: one factory in Korea ready for export with WHO PQ status, and one factory in India, which only produces for the Indian domestic market. The SD Bioline test is quoted at US\$1 per test,²⁴ which is more likely to fall in line with LMICs' health care budgets. Though RNA tests are more expensive than antibody tests, it is not appropriate to directly compare the unit costs of HCV antibody and RNA tests. Antibody testing can only identify which individuals have been exposed to HCV—antibody positive individuals still require confirmatory RNA tests for diagnosis. Therefore, a screening program in a population with a prevalence of 2% (1 out of 50) would need to invest US\$50 in antibody screen to identify one individual in need of a confirmatory RNA test.

23. Médecins Sans Frontières (MSF). Putting HIV and HCV to the test: a product guide for point-of-care CD4 and laboratory-based and point-of-care virological HIV and HCV tests, 3rd edition. 2017 July. https://www.msfacess.org/sites/default/files/HIV_Report_PuttingHIVHCVtotheTest_ENG_2017

24. *Ibid.*

25. Marinucci, F. Access to HCV diagnosis. Presentation at the World CAB meeting on HCV generics and diagnostics. 2017 July 18-20; Bangkok, Thailand.

26. Modified from Table 2, in Treatment Action Group. 2017 Pipeline Report. New York: Treatment Action Group; July 2017.

27. The Foundation for Innovative New Diagnostics (FINN). High-priority target product profile for hepatitis C diagnosis in decentralized settings: Report of a consensus meeting. 2015 April. <https://www.finddx.org/target-product-profiles/>

28. Médecins Sans Frontières (MSF). Putting HIV and HCV to the test: a product guide for point-of-care CD4 and laboratory-based and point-of-care virological HIV and HCV tests, 3rd edition. 2017 July. https://www.msfacess.org/sites/default/files/HIV_Report_PuttingHIVHCVtotheTest_ENG_2017

29. Genedrive. Genedrive HCV ID Kit Documentation. 2017 April. <https://www.genedrive.com/assays/hcv-documentation.php>

KEY MESSAGES

Key messages on HCV diagnostics from the community workshop centered on the need to develop literacy tools and build capacity. Such tools would serve to empower communities and treatment advocates; Support advocacy for:

- Increased pricing transparency and for securing price reductions on the different diagnostic tests (including through bundling procurement across diseases);
- Simplification of the HCV diagnosis algorithm and cure confirmation through removal of unnecessary tests from national guidelines;
- Better integration HCV testing into existing laboratory infrastructure for multi-disease platforms;
- Demand development of an HCV point-of-care tests that allow for rapid confirmation of viremia in decentralized settings by health care workers.

With actual program costs in mind, there remains an urgent need to expand the options in antibody testing to promote competition and price reductions.

Access to confirmatory RNA tests for chronic HCV infection and successful post-cure treatment is recognized as a barrier to scaling up testing and treatment services, particularly in remote settings as HCV RNA and cAg tests are not yet available in a reliable point-of-care platform.

Development of a commercial HCV core antigen point-of-care test to diagnose active infection with high specificity and high sensitivity is ongoing. Ideally, such a test would use capillary (finger stick) blood samples, provide results in less than 15 minutes, and cost less than US\$5 per test.²⁵ This technology could be targeted for use by community health workers and thereby allow for a scale up of decentralized testing approaches.

At present, the most flexible (i.e. for use outside of central laboratories) commercially available platform may be Cepheid's GeneXpert, a multi-disease platform machine that can run confirmatory tests on HIV, HCV, TB and other infectious diseases. Though the machine itself can test for multiple diseases, a disease-specific cartridge is required. GeneXpert is already used in 130 of the countries eligible for concessional pricing, primarily for TB and HIV diagnoses. If HCV programs can reach high testing volumes (i.e., increase the number of people tested), then prices could conceivably fall in line with per-test-prices for HIV cartridges. Cepheid has expressed openness to bundling volumes of national Ministry of Health orders for HIV and HCV, an option that should certainly be explored where Ministries of Health are procuring GeneXpert test cartridges for either disease.

TABLE 4 TARGET PRODUCT PROFILES FOR HCV DIAGNOSTICS^{26 27 28 29}

	OPTIMAL SPEC	MINIMAL SPEC	CEPHEID	MOLBIO	ABBOTT	ABBOTT	ALERE SD BIOLINE	ROCHE	GENEDRIVE
PRODUCT NAME	Prototype	Prototype	GeneXpert HCV RNA	Truenat HCV RNA	Architect core Ag	RealTime HCV RNA	SD Bioline HCV Antibody	Cobas HCV RNA	HCV RNA PoC
TARGET USERS	Community workers	Health care workers	Minimal	Optimal	Minimal	Minimal	Minimal	Minimal	Optimal?
SETTING	Community centers	District Hospitals (II)	PoC but somewhat centralized	Optimal	Minimal	Minimal	Optimal	Minimal?	Both
ANALYTICAL SENSITIVITY	200 IU/ml	1000 – 3000 IU/ml	Minimal?	?	Minimal	Minimal	?	Optimal for Quant	Yes
DIAGNOSTIC SENSITIVITY	>99%	>98%	Minimal?	?	Minimal	Minimal	>99%	Optimal?	TBD
POLYVALENCY	Platform allows HCV, HBV, HIV tests	Platform allows HCV, HBV, HIV tests	Yes	HIV	HIV	HIV, HCV genotyping	HIV	HIV	TBD
QUANTITATION	Quantitative	Qualitative	Optimal	Optimal	Minimal	Optimal	Optimal	Both	Approximate quantitative results
SPECIMEN TYPE	Capillary blood	Venous blood/plasma	Both	Both	Both	Both	Serum, Plasma, Whole blood 10uL	Both?	Both
STEPS	<2	2	Cartridge based	?	Cartridge based	Cartridge based	Cartridge based	?	~4
TIME TO RESULT	<15 mins	<60 mins	?	?	?	?	5-20 mins	?	<90mins
INSTRUMENT COST	<US\$2000	<US\$20,000	US\$18,000	?	€100,000?	?	?	?	?
ASSAY PRICE	<US\$5	<US\$15	<US\$20	US\$15?	?	US\$13-35	US\$15-25?	Depends on country; US\$35-45	?

The World CAB discussed the potential advantages of better integration of HCV testing into existing domestic multi-disease platform capacity, including limitations placed by international donors. It was also recognized that there is a great need for more companies to introduce such technologies. The fact that Cepheid has emerged as a dominant player in the multi-disease platform market was highlighted as a concern.

Epistem's Genedrive™ was CE marked in September 2017 but the platform was not in use in the field at press time. The platform can conduct RNA confirmation tests, and could conceivably be adapted for use in community centers or district hospitals. As with GeneXpert, the Genedrive platform offers the possibility of testing for drug-resistant TB, however at present, the drug-resistant TB Genedrive tests are only marketed in India.

Abbott's Architect™ comes in a RNA and cAg platform for centralized laboratory settings, so applicable for countries with high volume (e.g., up to 100 tests/hour) and for screening multiple diseases. The cAg platform does not work on dried blood spot samples.

Molbio/bigTech (Truenat™ PCR) is in the pipeline for 2017 or 2018. Wave 8D Biosciences (EOSCAPE HIV™) and Ustar (RT CPA) are developing HCV RNA platforms in 2019. Micronics (PanNAT™) is also developing an HCV qualitative platform in 2019. For cAg tests, Daktari™ is expected on the market in 2019.

The table 4 compares point-of-care tests currently in the field and in the pipeline based on FIND's Target Product Profiles.



MEETING PART TWO: COMMUNITY-GENERIC COMPANIES DIALOGUE

Prior to the meetings, each company was asked to provide a detailed overview of their clinical and access programs, including info on distribution arrangements, pricing, WHO prequalification, registration and export to selected countries (see table 5).

Recommended by EASL for the treatment of all six genotypes, sofosbuvir/daclatasvir (SOF/DCV) has been proven to be a highly effective and safe regimen. Of the companies present, only Hetero has developed SOF/DCV fix-dose combination (FDC), and none has submitted daclatasvir for the WHO prequalification. No clear answer on the reasons for those delays was provided, however, Hetero and Mylan both expressed commitment to expand access to DCV and SOF/DCV FDC.

The three generic companies—Hetero, Mylan and Pharco—committed to submit all their HCV portfolio to the WHO prequalification (WHO PQ). Activists expressed the concern that no company had submitted daclatasvir to WHO PQ yet, and the CAB demanded greater urgency.

As a follow up to the issue of pre-qualification, activists asked whether all generics were produced at the factories inspected as part of the pre-qualification process. Mylan committed to provide a single global quality across factories.

Activists expressed as take home message to generic manufacturers to accelerate registration of DAAs, including SOF/DCV FDC, across LMICs and to make all efforts to accelerate pre-qualification by the WHO.

WHEN VOLUNTARY LICENSES LOCK UP ACCESS IN EXCLUDED COUNTRIES

Hetero and Mylan have signed a voluntary license with Gilead on SOF, SOF/LED and SOF/VEL. They also have sub-license agreements with the Medicines Patent Pool for DCV. Both licenses exclude several dozen upper middle-income countries.

Both Mylan and Hetero stated they are pursuing registration of their products in the countries included in the VLs. They indicated they would agree to register and supply to an excluded country if it was to issue a compulsory license, but did not indicate if they would register and supply in excluded countries where there is no patent or where the patent has been opposed. For example, when Hetero representatives were asked if the company was interested in registering and exporting its products to Argentina—where there is no patent on SOF—they responded that the country is not included in the voluntary license and they need to stay compliant with the license.

Mylan stated their strategy for access in countries excluded from voluntary license, such as with Thailand³⁰ in regards to Gilead's license, was to attempt to get Gilead to expand the license, and called on the activists to do the same. Moreover, Mylan indicated that they would need to check with Gilead's legal team if they would be allowed to register and supply SOF in countries excluded from the license where there is no patent, like Argentina, or where the patent would have been effectively challenged.

Hetero and Mylan have a history of challenging Big Pharma's monopolies to increase access to affordable HIV treatment. However, in the case of DAAs the licensees have more passively accepted the market share conceded through VLs. This situation is concerning for access to affordable medicine across the globe, which historically has greatly benefited from having Indian generic manufacturers as allies which have been willing to support efforts to promote and support the use of TRIPS flexibilities.

Pharco has adopted a more confrontational attitude with regard to patent holders, stating they are closely following the patent opposition procedures and winning a court challenge against the originator company, Gilead, to gain market access in the Ukraine.

Activists expressed their strong concern that the existing VLs exclude dozens of middle-income countries, and call on generic manufacturers to register their products in all countries including those excluded from the VLs.

PRICING OF GENERIC DAAS

Hetero and Mylan failed to provide prices for their HCV treatment across LMICs or to clearly state their pricing policy; they only indicated that price would depend on volumes (i.e., high numbers of patients).

30. Please note that Mylan's statement was before Gilead extended its VL to include Thailand, in September 2017.

TABLE 5 GENERIC COMPANIES HCV PORTFOLIO AND INDICATED ACCESS POLICIES

	HCV PORTFOLIO	GLOBAL SALES (BOTTLES)	PRODUCTION OF API	WHO PREQUALIFICATION	REGISTRATION APPROVED (# COUNTRIES)	REGISTRATION PENDING (# COUNTRIES)	PRICE	ACCESS POLICY
HETERO	SOF	2016: 759,000 2015: 483,000	yes	Expected 2017	21	28	Not provided	Partnerships with CHAI (Quick Start program in Vietnam and Myanmar); Bilateral discussions with specific countries; Gilead treatment donation program.
	SOF/LED FDC		yes	Expect to file Q4 2017	11	14	Not provided	
	DCV		yes	Expect to file Q4 2017	8	22	Not provided	
	SOF/VEL FDC		yes	Expect to file 2018	1	2	Not provided	
	SOF/VEL/VOX	<i>Pipeline</i>	—	—	—	—	—	
	SOF/DCV FDC	<i>R&D</i>	—	—	—	—	—	
MYLAN	SOF	2016: 500,000	yes	Prequalified	16	19	Not provided	Training of service providers (Vietnam, Myanmar, Indonesia, Pakistan, Egypt), collaboration initiatives (HepBuzz, HepNet)
	DCV		yes	Received in Q3 2017	6	25	Not provided	
	SOF/LED FDC		yes	Expect to file Q4 2017	10	25	Not provided	
	SOF/DAC FDC	—	yes	Not indicated	0	Few	Not provided	
	SOF/VEL FDC	—	yes	Expect to file Q1 2018	Not indicated	Not indicated	Not provided	
	SOF/VEL/VOX	<i>Pipeline</i>	—	—	—	—	—	—
	G/P	<i>Pipeline</i>	—	—	—	—	—	—
PHARCO	SOF	2016: 1,500,000	yes	Expected 2017	Ukraine, Azerbaijan, Kirghizstan, Turkmenistan, Moldova, Kazakhstan, Rep. of Côte d'Ivoire, Cameroon, Sudan, Lebanon, Saudi Arabia	Ethiopia, Belarus, Vietnam, Uganda, Rwanda, Nigeria, Jordan	US\$294 per 12-week treatment (target retail price for SOF/RAV)	Tour n'Cure (international program for medical tourism); Voluntary license with for RDV
	RDV	<i>Phase II/III clinical trial</i>	—	—	—	—	—	—

Pharco indicated that their target price for SOF/RDV is US\$ 294 (including import and distribution markups) for a 12-week treatment.

Control over local distributors margins

In most countries where they export, generic companies operate through local wholesale or retailer distributors which charge a margin that can add significantly to the final price of a drug, particularly when one company has exclusive permission to distribute without competition. Activists expressed considerable concern to generic companies over excessive distributor margins in certain countries, such as Vietnam, where a single bottle of generic SOF ("MyHep") costs US\$ 600. In many countries, the result is that civil society organizations distribute drugs in order to cut out price-gouging middle agents.

Mylan and Hetero indicated that pricing policies of their local distributors were not entirely within their control. Mylan blamed it on the lack of awareness and expressed the need to increase volumes to get prices down, which will not necessarily solve the problem. The companies indicated they often have exclusive deals with local distributors covering different medicines, depriving them of control over retailing conditions for specific portfolios. However, Pharco was the exception, stating they enforce a price structure with a 20% limit on markups for distributors.

Activists stated that companies are risking their reputations by allowing local distributors to charge whichever price they choose, and cannot live up to their stated commitment to provide affordable generics if they abdicate responsibility for unaffordable retail prices.

Moreover, rather than waiting and expecting high volumes to reduce cost, if companies would enforce price control over distributors it would allow to reach higher volumes.

Activists called on generic manufacturers to regain control on pricing and make their treatments truly affordable.

Test and treat package

In India, due to competition in the HCV treatment market, companies are offering patients discounts for free HCV tests and ribavirin (RBV). Generic companies

could expand treatment access and find more patients by partnering with diagnostic test manufacturers to bundle testing and treatment packages for procurement. However, this should never result in substandard diagnosis for patients. The package must include an anti-HCV antibody test, at least two HCV RNA tests – for diagnosis and confirmation of cure (at SVR12) – as well as other recommended tests, and the most effective treatment option, thereby avoiding ribavirin whenever clinically possible.

ROLE OF ACTIVISTS AND COLLABORATION WITH GENERIC COMPANIES

The activists emphasized the importance of community advocacy and activism in facilitating access to treatment. Advocates play a significant role in guaranteeing the sustainability of generics in local markets by creating treatment demand through awareness, pushing governments to scale up testing and treatment, advocating for impacted communities and contributing to remove patent barriers on DAAs.

A constructive relationship between the World CAB and generic companies can be forged that would allow treatment advocates to share information on HCV prevalence, the patent landscape, legal and regulatory context, and treatment priorities among key populations in their countries, with the mutual goal to massively scale up testing and treatment.

Activists were disappointed that representatives from Mylan and Hetero were unable to directly answer many questions, including those sent to them ahead of the meeting, on company pricing and access strategy, whether because they lacked the knowledge or were unable to speak on behalf of the company. They were unaware of the HCV patent opposition landscape despite the fact that this is crucial for access to generic treatments. Mylan representatives expressed not being informed that a government had approached and started negotiating with the company; they were not able to provide the name of the local distributor or prices in Nepal. They were also unable to provide information on the implementation of anti-diversion policies by their company. Hetero representatives were not aware whether their company exported or intended to export active pharmaceutical ingredients for DAAs.

Those representatives committed to respond after the meeting with responses to the unanswered questions, however, no responses have been received to date.

TREATMENT

FOR ALL

MEETING PART THREE: COMMUNITY-DIAGNOSTIC COMPANIES

The three confirmed diagnostics companies—Alere, Cepheid, and Roche—were sent questions in advance that addressed the HCV diagnostics in their portfolios. Questions targeted information about their WHO PQ filings, pricing and access strategies in specific countries and/or across regions, and ways they are or could be supporting national surveillance systems. Participants had an opportunity to ask detailed questions about the technical aspects of the technologies and country-specific questions.

PRICING

Pricing of HCV diagnostic tests is a crucial issue given that, except for the anti-HCV antibody test that may be provided in HIV and harm reduction programs, most HCV diagnostic tests must be financed out-of-pocket.

Alere did not provide pricing transparency over its HCV test. Alere representatives said that the company has regional pricing standards with specific prices for certain countries, and negotiated prices for international programs, but did not disclose the specific pricing standards or the negotiated prices.

Roche specified that diagnostic machines can be provided for “free” with so-called reagent rental agreements, where equipment is placed free of charge in exchange for a guaranteed volume of reagent purchases. Prices depend on procurement volumes and vary

from US\$ 12/test to US\$ 40/test. It was also noted that bundled pricing across HIV and HCV tests may be offered, with offers depending on local procurement arrangements by Roche country offices.

Cepheid published their ceiling price and volume-based discount for HCV RNA cartridges within their so-called “non-commercial” program. The terms of this program extend to 120 High Burden Developing Countries (HBDC). One HCV RNA cartridge ranges from US\$ 17.10 (ceiling price) to US\$ 12.35 (for a minimum of 4,000,000 tests/year) (see Table Z). Cepheid allows volume aggregation across virology tests (HCV, HIV, HPV) and, potentially, across countries. Activists asked Cepheid to enable bundled procurement to include not just virology tests, but also orders of TB tests. This request stems from the fact that where GeneXpert machines are present, much of the capacity is currently dedicated to testing for confirmation of drug-resistant TB. Therefore, bundling would permit HIV and HCV programs to benefit from the bulk discounts offered via increased volumes. However, bundling HIV/HCV/HPV orders with TB orders is not possible yet.

In addition to the cartridges, countries must buy the Cepheid GeneXpert machines. The cost of a four-module machine, which can perform four tests at a time, is US\$ 17,000. However, these prices (for machine and cartridges) do not include shipping fees, customs fees, inventory fees, and/or distribution markups. Participants asked Cepheid to consider providing free machines to countries in order to increase the landscape of diagnostic facilities in LMICs, and to recover through a US\$ 1 increase of the cost of the cartridges—a practice adopted by other diagnostic companies, called reagent rental agreements. However, Cepheid currently refuses to use reagent rental agreements.

TABLE 6 CEPHEID HBDC VIROLOGY PRICING, 2016

PRICE/TEST	CEILING PRICE	500K TESTS/YR	1.0M TESTS/YR	1.5M TESTS/YR	3.0M TESTS/YR	4.0M TESTS/YR
HPV	\$16.70	\$15.40	\$15.15	\$14.45	\$12.40	\$11.35
HCV VL	\$17.10	\$16.43	\$15.65	\$15.16	\$13.45	\$12.35
HIV-1 VL	\$16.80	\$16.08	\$15.30	\$14.75	\$13.10	\$11.98
HIV-1 QUAL	\$17.95	\$14.43	\$16.65	\$16.08	\$14.45	\$13.35

- Discounts from the ceiling price will apply with volumes starting at 500K units per 12 months with a firm order.
- All of the above Virology menu above can be aggregated together for volume.
- Countries aggregated under one contract may benefit from discount.
- Prices follow Cepheid’s general HBDC terms and conditions (ex-works, prepaid in US\$).

The issue of markups to the price that the diagnostic company receives was an important discussion point at the World CAB. In many cases, HCV tests cost the final payer much more than the prices reported by companies. For example, in Vietnam, an HCV RNA test via a Roche machine costs US\$ 50. Company representatives argued that there can sometimes be a lack of harmony between global and country offices (Roche), and that procurement made through a local distributor could apply additional margins (Cepheid).

Just as the generic manufacturers must be held accountable for the final price of their products, diagnostic companies must be required to control their country offices and local distributors. This may be done by imposing caps on markups to ensure price control over their products. All diagnostic companies should provide transparency over their prices and volume-based discounts. Furthermore, government-imposed markups such as customs fees or value-added taxes may impose significant increases to the final price of both diagnostics and medicines.

USE OF EXISTING PLATFORMS

As the overwhelming majority of GeneXpert machines have been procured by TB and HIV programs, Cepheid was asked if they would refuse to guarantee the maintenance if a machine was used to diagnose a disease outside the mandate of the program that procured it. Cepheid responded that they are supporting the use of their machines for diagnostics across diseases and that it would not lead them to cancel the warranty or maintenance agreement.

DEVELOPMENT OF HCV CORE-ANTIGEN RDT AND OTHER HCV DIAGNOSTIC POC TESTS

Recently, Alere has been bought by Abbott, which markets an HCV core antigen test. Theoretically, a core antigen test could replace the HCV RNA test to confirm the active infection and post-treatment cure. As a substitute to RNA confirmation, the key issues for core antigen tests will be accuracy and affordability. Participants presented to the Alere representative a demand to develop an affordable HCV core antigen rapid diagnostic test (RDT), but he declined to comment on the progress of the HCV core antigen.

Discussions with Roche and Cepheid revealed different strategies for the development of point-of-care tests, a key component of decentralized models for testing. Cepheid is developing a GeneXpert (OMNI) that can be transported to remote areas and able to work on battery power. A limit of this technology is that only one test can be performed approximately every 90-105 minutes; faster analysis is needed in areas with high numbers of HCV-exposed individuals. Cepheid is also currently evaluating the efficacy of their HCV RNA test with finger stick (capillary) blood, which would facilitate the testing of people with vein damage, as well as task-shifting, or having non-medical personnel perform certain tasks in the community rather than in a centralized hospital or lab. The finger stick sample is expected to work on the GeneXpert machine with specific cartridges that should be available in 2018. Alternatively, Roche is investing in decentralized HCV diagnostics by developing technologies to enable easy transportation of blood samples from remote areas to laboratories.

SIMPLIFICATION OF HCV DIAGNOSTICS AND TREATMENT SUCCESS MEASUREMENTS

CAB participants also raised the issue of the cost of testing algorithms which require multiple HCV tests, as unnecessary tests present a bottleneck for access to treatment in certain LMICs. They expressed the need to shift toward simplified diagnostics and algorithms, emphasizing that the use of pangenotypic DAAs would avoid costly genotyping tests. The Roche representative referred to WHO guidelines to state that genotyping test still has a role, such as in countries without access to pangenotypic DAAs. While patients should have access to the most effective testing and diagnostic strategies and tools, companies' marketing strategies must not result in unaffordable and unnecessarily complex diagnostic algorithms.

CONCLUSIONS

The HCV World CAB meeting was the first time that community members met with both generics *and* diagnostics companies. The meeting addressed ways to scale up testing and generic treatment, in low- and middle-income countries. The advocacy workshops and in-person meetings deepened participants' technical knowledge and advanced advocacy strategies at national, regional, and global levels. While both generics and diagnostics companies provided limited concrete information on pricing (Pharco and Cepheid being the exceptions), the CAB provided an opportunity to exchange information with these companies and to assert the most pressing concerns that we face in our own countries.

The meeting taught a number of essential lessons as we forge ahead. There continues to be a lack of coordination and cohesive communication among treatment advocates and other civil society partners. Intersectionality—addressing overlapping structural injustices—is key. Through intersectional organizing and bridging with other social movements, such as with harm reduction, drug decriminalization, trade justice, labor/care work, and other public health efforts that go beyond HIV, HCV, or access to medicines—we will strengthen our efforts to mobilize our respective communities around the need to access information, and affordable HCV testing and generic treatments.

Time and resources should be allocated so that treatment advocates can share their common values, while recognizing the importance of tailoring access strategies in each country. There is a need for technical as well as funding support for smaller, resource-limited countries which do not have generic production or distribution capacity. Finally, activists in the global North or international organizations must listen to activists in the global South and support their efforts, upon request.

The discussion left us with few illusions that the task before us will be easy. A sober analysis of the barriers to elimination show the scale and scope of work that remains. Though not an exclusive list, the following challenges were highlighted: many treatment advocates and people living with HIV and/or HCV face increasingly turbulent political challenges, with the

emergence of more conservative governments that favor the criminalization of drugs and the people who use them. Moreover, there is an urgent need to overcome the stigma and discrimination toward people living with HCV and to promote awareness, using various media as an effective tool to reach people. HCV programs have become cash-strapped due to financial austerity and restrictions imposed by major donor organizations, which do not permit the treatment of HCV mono-infected populations. There is also a lack of pricing regulations to ensure consistency of drug prices within regions, and there is a backlog of registration for the latest HCV DAAs. Furthermore, lack of political commitment to eliminating this disease and absence of national HCV testing and treatment guidelines will derail efforts to increase diagnosis, reduce new infections, and increase treatment starts.

With these barriers in mind, several priorities for advancing efforts to eliminate HCV were identified:

- Simplification of treatment and diagnostic algorithms through a combination of affordable, high-quality point-of-care tests, and access to pangenotypic regimens;
- Reduction of prices on diagnostics (e.g., cartridge, test, and reagent);
- Expansion of options for diagnostics technologies that combine with HIV/TB to test for more HCV, as well as commitment by national labs to put this integration into practice;
- Removal of patent or other barriers to affordable treatment access, including middle-agent markups;
- Advocacy toward established TB/HIV donors to invest more in scale up of HCV diagnosis and treatment (e.g., Global Fund, PEPFAR, USAID), with particular consideration for HIV/HCV co-infected populations;
- Advocacy for “test-and-treat” approach that ensures treatment for all who need it;
- Technical support for advocates for forming and participating in steering committees to develop national testing and treatment guidelines.

This report has aimed to capture the developments in testing and treatment options since the first HCV World CAB, to highlight the diverse set of challenges that the community faces, and to summarize takeaways from the July 2017 World CAB in Bangkok. As a mere handful of the thousands of activists fighting to overcome the barriers to hepatitis C treatment, the latest World CAB has provided but a glimpse into the huge reserve of solidarity and commitment that the movement has built.

HCV activism has made significant progress in a comparatively short window of time since 2014. Through the application of frameworks and lessons developed from the HIV movement, hundreds of thousands of people have already accessed generic versions of novel DAA treatments.^{31 32} However, the vast majority of persons living with hepatitis C await treatment. And while awareness and affordable diagnostics remain huge barriers, the presence of monopoly-enabled prices will continue to remain a principal barrier for tens of millions of patients.

In short, the fight—whether against or in collaboration with other stakeholders—will certainly continue. The World CAB provided an opportunity to reiterate what activists have long advocated: the elimination of stigma and the right to health are fundamental ingredients to the successful response to any disease.

31. Freeman J, Khwairakpam G, Dragunova J, et al. 94% SVR with parallel imported generic direct acting antiviral treatment for hepatitis C. Poster presented at 52nd International Liver Congress, 2017 April 19-21; Amsterdam, Netherlands.

32. Hill A, Dragunova J, Korologou-Linden R, et al. Virological response rates using generic direct acting antiviral treatment for hepatitis C, legally imported into Russia. Poster presented at 52nd International Liver Congress, 2017 April 19-21; Amsterdam, Netherlands.

APPENDIX

APPENDIX A. SELECTION PROCESS

COMMUNITY PARTICIPANTS

In April 2017, the co-convenors sent an invitation for applications via email and listservs to global HCV, HIV, and access to medicines networks. Independent reviewers from Coalition PLUS, Médecins du Monde, and Treatment Action Group selected the World CAB participants through a review of de-identified applications, designed to achieve regional and gender balance. The set of scoring criteria, modeled after those used for previous CABs, prioritized the following special populations:

- People living with HIV and/or HCV
- People who inject or use drugs
- People who were previously incarcerated or working with prisoners
- Men who have sex with men.

PHARMACEUTICAL COMPANIES

After consultation with partners at Asia-Pacific Network of People Living with HIV/AIDS (APN+), Drugs for Neglected Diseases Initiative (DNDi), International Treatment Preparedness Coalition (ITPC), Médecins Sans Frontières (MSF), TREAT Asia, and Ukraine Alliance for Public Health companies prioritized to invite to the World CAB were:

- Generic companies with finished-product formulation of DAAs or which produced active pharmaceutical ingredients (APIs), which submitted for World Health Organization (WHO) pre-qualification and/or were actively or considering exporting generics to other LMICs
- Diagnostics companies with HCV tests or assays in use in the field.

APPENDIX B. WORLD CAB PARTICIPANTS

ASIA-PACIFIC

Binod Gurung

SATHI SAMUHA, Nepal

Chalerm Sak (Jockey) Kittittrakul

AIDS Access Foundation, Thailand

Edo Nasution, Persaudaraan Korban

NAPZA Indonesia/Indonesian Drug Users Network (PKNI), Indonesia

Edward Low

Positive Malaysian Treatment Access & Advocacy Group, Malaysia

Giten Khwairakpam

TREAT Asia, Thailand

Harry Prabow

Asia-Pacific Network of People Living with HIV/AIDS (APN+), Thailand

Himal Gauchen

Union C, Nepal

Jirasak Sriparmong

Thai AIDS Treatment Action Group, Thailand

Kajal Bhardwaj

Intellectual Property Lawyer/Consultant, India

Khaing Thandar Hnin

Médecins du Monde, Myanmar

Mathilde Laval

Médecins du Monde, Vietnam

Omar Syarif

Asia-Pacific Network of People Living with HIV/AIDS (APN+), Thailand

Paul Lhungdim

Delhi Network of Positive People (DNP+), India

Rajkumar Komolkjit Singh

Community Network for Empowerment (CoNE), India

Saeed Hamd

Aga Khan University, Pakistan

Shiba Phurailatpam

Asia-Pacific Network of People Living with HIV/AIDS (APN+), Thailand

Tran Viet Phong

Center for Supporting Community Development Initiatives, Vietnam

EASTERN EUROPE**Sergey Golovin**

International Treatment Preparedness Coalition Russia (ITPCru), Russia

HIGH-INCOME COUNTRIES**Annette Gaudino,**

Treatment Action Group, United States

Bryn Gay

Treatment Action Group, United States

Céline Grillon

Médecins du Monde, France

Chase Perfect

Coalition PLUS, France

Francesco Marinucci,

Foundation for Innovative New Diagnostics (FIND), Geneva

Isaac Chikwanha

Médecins Sans Frontières, Geneva

James Freeman

FixHepC, Australia

Jean Luc El-Kaim

Coalition PLUS, France

Jean-Michel Piedagnel,

Drugs for Neglected Diseases Initiative, France/Malaysia

Marie Missioux

Médecins du Monde, France

Navneet Singh Tewatia

FIND, Geneva/India

Priti Radha Krishtel

Initiative for Medicines, Access and Knowledge (I-MAK), United States

LATIN AMERICA**Agustina Lazcano**

Fundación Grupo Efecto Positivo, Argentina

Francisco Rossi

IFARMA Foundation, Colombia

Lorena Di Giano

Fundación Grupo Efecto Positivo & Red Latinoamericana por el Acceso a Medicamentos (RedLAM), Argentina

Sara Helena Pereira e Silva

Universities Allied for Essential Medicines, Brazil

MIDDLE EAST AND NORTH AFRICA**Khaoula Hajarabi**

Association de Lutte Contre le Sida, Morocco

Zniber Mohamed Hajji

International Treatment Preparedness Coalition – MENA (ITPC MENA)

SUB-SAHARAN AFRICA**Abigael Lukhawro**

Médecins du Monde, Kenya

APPENDIX C. PHARMACEUTICAL COMPANY REPRESENTATIVES**GENERIC COMPANIES****HETERO****Madhura Marathe**

Product Executive, International Marketing, India

Shailesh Pednekar

Senior Vice President, International Marketing, India

MYLAN**Jirasak Phisitsak**

Country Head, Thailand

Preet Kamal Singh

Assistant General Manager, BD and Strategy,
Emerging Markets, India

PHARCO**Dr. Sherine Hassan Abbas Helmy**

Vice President, Egypt

Dr. Yasser Fayed

Director, Business Development, Egypt

DIAGNOSTICS COMPANIES**ALERE****Siddharth Singh**

APAC Marketing Manager (Infectious Disease), United
States/Singapore

Vinay K

APAC Marketing Director, United States/Singapore

CEPHEID**Iain Sharp**

Director, TB & Virology, Global Marketing, United
States

Martin Colla

Programme Director Asia, High Burden & Developing
Countries, United States

ROCHE**Maciej Maniecki**

Senior International Product Manager, HCV/Virology,
Switzerland

APPENDIX D. MEETING AGENDA

TUESDAY, 18 JULY 2017 (DAY 1)

- 08:30-09:15 Opening and Welcome (Shiba Phurailatpam, APN+ and Annette Gaudino, TAG)
- 09:15-10:00 Global HCV Context (Céline Grillon, MdM)
- 10:00-11:30 Discussion on access to HCV Direct-acting Antivirals
HCV DAA Pipeline (Annette Gaudino, TAG)
Access to HCV DAAs (Isaac Chikwanha, MSF)
Patent Barriers to HCV DAAs (Priti Krishtel, I-MAK)
- 11:30-12:30 Discussion on access to HCV Diagnostics
HCV Diagnostics Landscape (Francesco Marinucci, FIND)
- 12:30-13:30 Lunch
- 13:30-14:45 Civil Society Experiences of In-country Advocacy
Enhancing Health Promotion to Enhance HCV Care Among People Who Inject Drugs (Edo Agustian, Persaudaraan Korban NAPZA Indonesia/Indonesian Drug Users Network [PKNI])
Screening and Testing in Thai Drop-in Centers (Jirasak Sripramong, Thai Treatment Action Group)
Update on Global Fund HCV Advocacy (Shiba Phurailatpam and Omar Syarif, APN+)
- 14:45-15:30 Break Out Groups
- 15:30-17:30 Experiences from Previous CABs (Sergey Golovin, ITPC-ru)

WEDNESDAY, 19 JULY 2017 (DAY 2)

- 08:30-10:15 Overview of Messaging
- 10:15-10:30 Coffee break
- 10:30-12:00 Meeting with Mylan
- 12:00-13:00 Lunch
- 13:00-14:30 Video Call with Hetero
- 14:30-14:45 Coffee break
- 14:45-16:15 Meeting with Alere
- 16:15-17:30 Debriefing and wrap-up

THURSDAY, 20 JULY 2017 (DAY 3)

- 08:30-09:15 Review of Messaging
- 09:15-10:45 Meeting with Cepheid
- 10:45-11:00 Coffee break
- 11:00-12:30 Meeting with Roche
- 12:30-13:00 Discussion on Follow Up Activities
- 13:00-14:00 Lunch
- 14:00-15:30 Video Call with Pharco
- 15:00-15:30 Debriefing and Closing

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