

Velásquez, Germán

Research Report

Access to Hepatitis C treatment: A global problem

Research Paper, No. 77

Provided in Cooperation with:

South Centre, Geneva

Suggested Citation: Velásquez, Germán (2017) : Access to Hepatitis C treatment: A global problem, Research Paper, No. 77, South Centre, Geneva

This Version is available at:

<https://hdl.handle.net/10419/232195>

Standard-Nutzungsbedingungen:

Die Dokumente auf EconStor dürfen zu eigenen wissenschaftlichen Zwecken und zum Privatgebrauch gespeichert und kopiert werden.

Sie dürfen die Dokumente nicht für öffentliche oder kommerzielle Zwecke vervielfältigen, öffentlich ausstellen, öffentlich zugänglich machen, vertreiben oder anderweitig nutzen.

Sofern die Verfasser die Dokumente unter Open-Content-Lizenzen (insbesondere CC-Lizenzen) zur Verfügung gestellt haben sollten, gelten abweichend von diesen Nutzungsbedingungen die in der dort genannten Lizenz gewährten Nutzungsrechte.

Terms of use:

Documents in EconStor may be saved and copied for your personal and scholarly purposes.

You are not to copy documents for public or commercial purposes, to exhibit the documents publicly, to make them publicly available on the internet, or to distribute or otherwise use the documents in public.

If the documents have been made available under an Open Content Licence (especially Creative Commons Licences), you may exercise further usage rights as specified in the indicated licence.



**SOUTH
CENTRE**

Research
Paper
May 2017

77

ACCESS TO HEPATITIS C TREATMENT: A GLOBAL PROBLEM

Germán Velásquez



RESEARCH PAPERS

77

ACCESS TO HEPATITIS C TREATMENT: A GLOBAL PROBLEM

Germán Velásquez^{*}

SOUTH CENTRE

MAY 2017

^{*} Germán Velásquez is Special Advisor on Health and Development at the South Centre, Geneva. I want to express my gratitude to Pascal Boulet, Graciela Diap, Carlos Correa, Viviana Muñoz and Chase Perfect for their comments and suggestions during the writing and revision of this paper. The author is however solely responsible for the content of this paper.

THE SOUTH CENTRE

In August 1995 the South Centre was established as a permanent inter-governmental organization of developing countries. In pursuing its objectives of promoting South solidarity, South-South cooperation, and coordinated participation by developing countries in international forums, the South Centre has full intellectual independence. It prepares, publishes and distributes information, strategic analyses and recommendations on international economic, social and political matters of concern to the South.

The South Centre enjoys support and cooperation from the governments of the countries of the South and is in regular working contact with the Non-Aligned Movement and the Group of 77 and China. The Centre's studies and position papers are prepared by drawing on the technical and intellectual capacities existing within South governments and institutions and among individuals of the South. Through working group sessions and wide consultations, which involve experts from different parts of the South, and sometimes from the North, common problems of the South are studied and experience and knowledge are shared.

NOTE

Readers are encouraged to quote or reproduce the contents of this Research Paper for their own use, but are requested to grant due acknowledgement to the South Centre and to send a copy of the publication in which such quote or reproduction appears to the South Centre.

The views expressed in this paper are the personal views of the author and do not necessarily represent the views of the South Centre or its Member States. Any mistake or omission in this study is the sole responsibility of the author.

South Centre
Ch. du Champ d'Anier 17
POB 228, 1211 Geneva 19
Switzerland
Tel. (41) 022 791 80 50
Fax (41) 022 798 85 31
south@southcentre.int
www.southcentre.int

TABLE OF CONTENTS

ABSTRACT	1
I. GENERAL CONTEXT AND BACKGROUND ON THE DEBATE OVER ACCESS TO MEDICINES	1
I.1. Problems of the R&D Model	2
<i>I.1.1 Lack of transparency of R&D costs</i>	<i>3</i>
<i>I.1.2. Pharmaceutical innovation has significantly diminished in recent years</i>	<i>3</i>
<i>I.1.3. High prices restricting access</i>	<i>3</i>
I.2. What Has Changed in the Last Two Years?	4
I.3. A Paradigm Shift in the Debate on Access to Medicines: 2014-2016.....	5
II. THE HEPATITIS C VIRUS: FIGURES AND DATA	6
II.1. What are Hepatitis C Genotypes?	6
II.2. Why do HCV Genotypes Matter?	7
II.3. Where are the HCV Genotypes Found?	7
III ACCESS TO HEPATITIS C TREATMENT	8
III.1. The New Direct-Acting Antiviral Treatments	8
III.2. Essential Medicines that Cure.....	8
III.3. Sofosbuvir: Between Financial Engineering and Public Health.....	9
III.4. HCV Diagnosis	10
III.5. World Health Organization Standardized Treatment Guidelines	12
III.6. The Sofosbuvir Patents	12
III.7. Oppositions to the Sofosbuvir Patent of Gilead.....	13
III.8. Voluntary Licenses Granted by Gilead.....	14
III.9. Anti-diversion Measures	15
IV. HOW TO OVERCOME THE BARRIERS TO ACCESS USING TRIPS FLEXIBILITIES.....	17
IV.1. Information on International Prices	17
IV.2. Adoption of Patentability Criteria from a Public Health Perspective.....	18
IV.3. Compulsory Licenses – Aspects and Practical Procedures.....	19
<i>IV.3.1. Identify relevant patents</i>	<i>19</i>

<i>IV.3.2. Explore possible sources of supply based on local production.....</i>	<i>19</i>
<i>IV.3.3. Identify possible sources of importation of the required medicines</i>	<i>20</i>
<i>IV.3.4. Marketing approval</i>	<i>20</i>
<i>IV.3.5. Request for a compulsory license</i>	<i>20</i>
<i>IV.3.6. Granting of the compulsory license by the competent department.....</i>	<i>21</i>
<i>IV.3.7. Negotiation with patent holder about royalty rate</i>	<i>21</i>
<i>IV.3.8. Determination of royalty fee by the Patent Administration Department..</i>	<i>21</i>
<i>IV.3.9. Appeal</i>	<i>22</i>
<i>IV.3.10. Other considerations.....</i>	<i>22</i>
V. SOME COUNTRIES HAVE LAUNCHED THE NEW HCV TREATMENT	23
CONCLUSIONS	25

“Viral hepatitis is an international public health challenge, comparable to other major communicable diseases, including HIV, tuberculosis and malaria. Despite the significant burden it places on communities across all global regions, hepatitis has been largely ignored as a health and development priority until recently”.¹

ABSTRACT

This document will address five items: 1) General context and background on the debate over access to medicines. 2) The problem of the Hepatitis C virus (HCV): Figures and data. 3) Access to new direct-acting antiviral (DAA) treatments for Hepatitis C. 4) How to overcome barriers to access: using the flexibilities of the TRIPS Agreement. 5) Some examples of countries that have launched the new HCV treatment and Conclusions.

I. GENERAL CONTEXT AND BACKGROUND ON THE DEBATE OVER ACCESS TO MEDICINES

The problem of access to medicines until 2014 was concentrated in developing countries where one third of the world’s population had no access to medicines, while industrial countries, thanks to public (Europe) and private (the USA) insurances managed to pay the cost of medicines. Currently the situation in developing countries remains the same but the great novelty, unprecedented, is that the industrialized countries are beginning to have difficulties in ensuring the supply of certain medicines to their citizens.

The debate and international negotiations on access to medicines began in 1995 with the creation of the World Trade Organization (WTO), at the end of the Uruguay Round, and the generalization of the mandatory use of patents for pharmacological products for all WTO member countries (currently totalling 162).

During the last 20 years (1996-2016), several important moments have marked the progress of the debate:

¹ WHO, Global Health Sector strategy on viral Hepatitis 2016-2021: Towards ending viral hepatitis, available from: <http://apps.who.int/iris/bitstream/10665/246177/1/WHO-HIV-2016.06-eng.pdf>.

- 1995 Creation of WTO and with it the mandatory adoption of the TRIPS Agreement.
- 1996 World Health Assembly Resolution 49.14 on “Revised Medicine Strategy”.
- 1997 “The WHO Red Book” on Globalization and access to medicines.
- 2001 (April) the South-African case² in which 39 pharmaceutical companies lost a suit that sought to denounce the medicine law developed by the Mandela government. (June) The African Group of the WTO requests a debate on access to medicines. (Nov.) The DOHA declaration on Public Health and Intellectual Property.
- 2002 British Government Report on Intellectual Property and Development.
- 2006 WHO report on Intellectual Property and Public Health, known most widely by its English acronym CIPIH.
- 2008 Global Strategy on Medicines and Intellectual Property negotiated and approved by the WHO member states.
- 2012 “CEWG”, a WHO report, recommends an international treaty on R&D.
- 2013 (May) WHO demonstration projects: a distracting exercise?
- 2016 High-level Panel of the Secretary-General of the United Nations on Access to Medicines.

I.1. Problems of the R&D Model

Let us recall that the current R&D model² for pharmaceutical products is based on the following scheme:

Research (*private or public*) – patent – monopoly – high price – restricted access



This model contains several contradictions and problems that in the long run lead to a disarticulation between innovation and access. We will briefly refer here to three problems or faults of the current R&D model:

- Lack of transparency of R&D costs.
- Pharmacological innovation has effectively diminished in the last years.
- High prices restricting access.

² Model that must obligatorily follow all members of the World Trade Organization nowadays.

1.1.1. Lack of transparency of R&D costs

The cost, reported in 2014 by a study of Boston Tufts Center, for the development of a new molecule was of **2.5 Billion US\$**.³ This is the figure currently used by the so-called originator pharmaceutical industry (i.e. “big Pharma”). However, in a study carried out by the London School of Economics in 2011⁴, the authors claim that the average cost to develop a new product is only 43.4 million US\$.

The non-profit foundation DNDi (Drugs for Neglected Diseases initiative) reported in 2013 that the average cost for research and development (R&D) of the **new chemical entities** that it had developed in its last 10 years of existence was between **100 and 150 million Euros**.⁵

As long as there is no clarity on the real cost of R&D, the problem of prices—and therefore of access to medicines—will continue to go unsolved. The massive difference between the estimates of 150 million US\$ or 2.5 Billion US\$ per molecule is significant, as the resulting price of the medicine would be significantly different.

1.1.2. Pharmaceutical innovation has significantly diminished in recent years

According to the data published by the French review *Prescrire* in recent years,⁶ we find that the number of medicines that constant “an important therapeutic advance” introduced into the French market in the last 10 years are not more than 14 per year; furthermore, innovation appears to be diminishing, as the maximum number of 14 is significantly higher than the average number of yearly therapeutic advances over the past decade:

- 2007: 14 products
- 2008: 6 products
- 2009: 3 products
- 2010: 3 products
- 2011: 3 products
- 2012: 3 products
- 2013: 6 products
- 2014: 5 products
- 2015: 5 products
- 2016: 5 products

1.1.3. High prices restricting access

In 2014, the American firm Gilead Sciences introduced the hepatitis C drug Sofosbuvir (brand name Sovaldi) at the eye-watering price in the USA of 84,000 US\$, 57,000 Euros, for a 12-week treatment.

³ Tufts Center for the Study of Drug Development, “Cost of developing a new drug” Boston, November 2014. http://csdd.tufts.edu/files/uploads/Tufts_CSDD_briefing_on_RD_cost_study_-_Nov_18,_2014..pdf.

⁴ Donald W. Light and Rebecca Warburton “Demythologizing the high costs of pharmaceutical research”, http://www.pharmamyths.net/files/Biosocieties_2011_Myths_of_High_Drug_Research_Costs.pdf.

⁵ DNDi, “Research & Development for Diseases of the Poor: A 10-Year Analysis of Impact of the DNDi Model”, Geneva 2013.

⁶ Rev. *Prescrire*, “L’année 2016 du médicament: un système qui favorise l’imitation plutôt que la recherche de réels progrès.” Paris, Page 136 Tome 37 No. 400.

A recent study in the United States of America indicates that out of the 71 anti-cancer medicines registered between 2002 and 2014 by the FDA, many of them cost more than 100 US\$ per treatment.⁷

Lack of transparency in the costs of R&D, a diminishing rate of pharmaceutical innovation in recent years and high prices all contribute to restrict access in both developing countries and developed ones. Collectively, these dynamics demonstrate a structural problem of the current R&D model for pharmaceutical products. Several documents discussed in the frame of WHO in the last 10 years, as well as a large number of studies and articles produced by scholars point to the existence of an incoherence in the R&D model.

At the end of 2015, the Secretary General of the United Nations issued a call for a High-Level Panel on Access to Medicines; the panel would be constituted by an array of international experts of demonstrated competence. The terms of reference set for the expert group called for a study on “**The incoherence between the rights of inventors, international human rights legislation, trade rules and public health**”. In less than three months, more than 180 proposals were submitted by a wide range of stakeholders: governments, institutions, UN agencies, NGOs, universities, pharmaceutical industries and individuals.

The received proposals can be summarized into five categories:

- 1) Comments on the current R&D model. (40)
- 2) Proposals to strengthen Health Systems. (27)
- 3) Proposals to progressively modify the R&D model. (46)
- 4) Contributions proposing a significant reform of the model. (46)
- 5) Other.

Government proposals included submissions by Holland, Lesotho, Japan and Jordan.

Among the main points of the report by the United Nations Secretary-General (issued in September 2016), the following recommendations may be highlighted:

- Use the available room provided by article 27 of the TRIPS Agreement to apply rigorous definitions of invention and patentability.
- Adopt and implement legislations to support Compulsory Licenses (CL).
- Review the decision on paragraph 6 of the Doha Declaration
- Refrain (governments and private sector) from any threats that may hinder the right to use TRIPS flexibilities
- Initiate a process (conducted by the UN-SG) to encourage governments to negotiate (...) a compulsory Convention for R&D.

I.2. What Has Changed in the Last Two Years?

The main new development is that the problem has now become global, involving both developing and developed countries. The totality of WHO documents and resolutions had previously referred to “diseases disproportionately affecting developing countries”. The

⁷ Jama: <http://jamanetwork.com/journals/jamaoncology/article-abstract/2497879>.

distinction between communicable and non-communicable diseases, implied an understanding that only communicable diseases were affecting developing countries. However, nowadays, non-communicable diseases also represent a substantial source of morbidity and mortality for developing countries.

For the first time in history, there are medicines that industrialized countries cannot afford to pay; this is demonstrated by, to cite just two examples, their adoption of policies that effectively ration newer medicines against Hepatitis C and medicines against cancer.

The Human-Rights Commission of the United Nations tackles the issue from a human rights approach rather than a trade approach. In their 2015 deliberations, the Human-Rights Commission considered that access barriers to these medicines could be considered a human rights violation.⁸

I.3. A Paradigm Shift in the Debate on Access to Medicines: 2014-2016

Three elements mark a paradigm shift in the debate on access to medicines: First: **a medicine that heals...** the efficacy of Sofosbuvir (and other direct-acting antivirals, known today under their English acronym, DAAs), stands in contrast to the vast majority of medicines that entered the market over the last 20 years. Second: **the inaccessible price** both for Northern and Southern countries has created a global problem. Third important element: **pharmaceutical industries dissociate cost and price** arguing that the price should be related to the paying capabilities of the country⁹ or to the “value” of the medicine as compared to the potential cost of treating sequelae such as a liver transplant operations or liver cancer treatments, as was recently the case with the medicine against Hepatitis C: Sofosbuvir.

The pharmaceutical industry business model has changed. Previously, high R&D costs were being claimed (sometimes quite artificially) to establish high prices and increase profits. Nowadays the pharmaceutical industry, and this is precisely the case of Gilead, are, above all, financial industries whose first goal is to remunerate their shareholders and have managed what scholars and civil society organizations had been claiming for years, to de-link R&D costs from the final price of the product. However, the industry has attempted to co-opt this term by twisting the meaning. As Ruth Dreifuss expressed in the Graduate Institute of Geneva on the 23rd of February, 2017, the industry’s twist on the concept suggests a “malefic de-linkage” through which cost and final price are unrelated and no attempt is made to reconcile the two. Instead, the price is calculated by the estimated “value” as argued by the producer or by the buyer’s purchasing power. As evidence of the latter, Gilead established a price of 84,000 US\$ in the USA for a 12 week treatment, while charging 900 US\$ in Egypt for the same medicines.

⁸ HRC Resolution on “Access to medicines in the context of the right of every one to the enjoyment of the highest attainable standard of physical and mental health”, Geneva, 2016.

⁹ Cf. Pratap Chatterjee, “Gilead Sciences Under Investigation for Over Charging for Hepatitis C Pil, <http://www.corpwatch.org/article.php?id=15964>.

II. THE HEPATITIS C VIRUS: FIGURES AND DATA^{10/11}

- Hepatitis C is a liver disease caused by the virus of the same name: the virus can cause both acute and chronic hepatitis infection, ranging in severity from a mild illness lasting a few weeks to a serious, lifelong illness that can cause death.
- According to the World Health Organization (WHO), it is estimated that globally approximately 130 million to 150 million¹² people live with a chronic hepatitis C virus (HCV) infection and it is estimated that 700,000 people die each year from hepatitis C-related liver diseases.
- The hepatitis C virus is a blood-borne virus and the most common modes of infection are through unsafe injection practices, inadequate sterilization of medical equipment, and the transfusion of unscreened blood and blood products.
- HCV can also be transmitted sexually and can be passed from an infected mother to her baby; however these modes of transmission are much less common.
- Hepatitis C is not spread through breast milk, food, water or by casual contact such as hugging, kissing and sharing food or drinks with an infected person.
- New types of treatment and oral therapeutic regimens named Direct Action Antivirals (DAAs) may heal more than 90 per cent of Hepatitis C infection cases.
- Currently there is no vaccine for hepatitis C.
- Hepatitis C virus (HCV) causes both acute and chronic infection. Acute HCV infection is usually asymptomatic, and is only very rarely associated with life-threatening disease. About 15–45 per cent of infected persons spontaneously clear the virus within 6 months of infection without any treatment.
- The remaining 55–85 per cent of persons will develop chronic HCV infection, and in these cases the risk of cirrhosis of the liver is between 15–30 per cent within 20 years. According to WHO, an estimated 2.9 millions of people living with HIV are infected with hepatitis C virus.¹³
- There are numerous HCV strains (or genotypes), variously distributed depending on the region.

II.1. What are Hepatitis C Genotypes?

Genotypes of the hepatitis C virus are different strains of the virus. Each strain differs from each other and can be distinguished by laboratory tests. Different genotypes are more common in some parts of the world.

Globally, there are 6 HCV genotypes, although some others are being studied. They are identified by a number, for example genotypes 1 to 6. There are also subtypes, identified by a letter (for example, genotype 1a).

¹⁰ WHO Facts sheet: <http://www.who.int/mediacentre/factsheets/fs164/en/>.

¹¹ Ref. International Association of providers of Aids Care: http://www.aidsinfonet.org/fact_sheets/view/674.

¹² This data has been revised by WHO and the estimation is now 70 million.

¹³ WHO, Global Health Sector strategy on viral Hepatitis 2016-2021: Towards ending viral hepatitis. <http://apps.who.int/iris/bitstream/10665/246177/1/WHO-HIV-2016.06-eng.pdf>, p. 11.

II.2. Why do HCV Genotypes Matter?

The different HCV genotypes generally act similarly in how they infect people and cause disease; they are important for vaccine development, for the progression of hepatic fibrosis and to evaluate the response to antiviral treatments.¹⁴

II.3. Where are the HCV Genotypes Found?

Genotypes 1, 2 and 3 are present all over the world. Subtypes 1a and 1b are the most common ones, representing approximately between 60 per cent and 70 per cent of global infections. Genotype 1a can be found primarily in North and South America, Europe and Australia, while type 1b is found in North America, Europe and parts of Asia.

Genotype 2 occurs in most developed countries but is much less common than genotype 1. Genotype 3 is common in Southeast Asia but can also be found in other countries.

Genotype 4 can be found primarily in the Middle East, Egypt and Central Africa. Type 5 is found in South Africa and in local groups around the world, which, in general, results in a small number of infected individuals.

¹⁴ Lee CM, Hung CH, Lu SN, Changchien CS. *Chang Gung Med J*. "Hepatitis C virus genotypes: clinical relevance and therapeutic implications. Review" 2008 Jan-Feb;31(1):16-25.

III ACCESS TO HEPATITIS C TREATMENT

III.1. The New Direct-Acting Antiviral Treatments

Until the end of 2013, the standard treatment for Hepatitis C consisted of pegylated interferon injections over 24 to 48 weeks and complemented with ribavirin tablets twice a day. This treatment was costly, toxic, complicated to administer and with healing rates of less than 50 per cent.¹⁵

In late 2013, a new Hepatitis C treatment called direct-acting antivirals (or DAAs) was introduced in the market. In eight to twelve weeks of treatment these medicines could heal more than 90 per cent of persons with a chronic HCV infection.

The new DAAs treatments were introduced by the firms Gilead Sciences and Bristol Meyer Squib (BMS) in 2014. Gilead has patented or applied for patents for three DAA compounds: sofosbuvir, ledipasvir and velpatasvir.¹⁶ BMS has patented or applied for a patent on daclatasvir.¹⁷ As treatment in many cases must include both sofosbuvir and daclatasvir it means that there is a double barrier, two or more patents belonging to different firms. Other transnational firms such as AbbVie and Janssen have also put DAAs on the market, while additional products are in the “pipeline” of these and other firms. However, for the foreseeable future, sofosbuvir will likely remain the dominant DAA.

The first DAA launched by the North American firm Gilead Sciences, sofosbuvir, was put on the market at the exorbitant price of 84,000 US dollars for a twelve-week treatment.

According to WHO,¹⁸ in 2015 (two years after the first DAAs came out), of the estimated 130 to 150 million people living with HCV only 275,000 persons received the new DAAs treatment, from which 170,000 were patients in Egypt, which is the country with the largest prevalence of Hepatitis C in the world. This was possible, as we shall see later, thanks to the fall of 12-week treatment prices from 900 to 153 US\$, instead of the 84,000 US\$ that Gilead originally demanded.

III.2. Essential Medicines that Cure

As reported by Professor Philippe Even, there have only been a limited number of curative medicines launched by the pharmaceutical industry in the last 20 years.¹⁹ The new orally-administered DAA medicines are effective and until now appear to be well tolerated. Cure rates, defined formally by spontaneous viral clearance or SVR, figures after a 12-week

¹⁵ Manns MP, Wedemeyer H, Cornberg M. “Treating viral hepatitis C: efficacy, side effects, and complications”. *Gut* 2006;55(9):1350-9.

¹⁶ Gilead Sciences, 2016 <http://investors.gilead.com/phoenix.zhtml?c=69964&p=irol-irhome>.

¹⁷ MSF briefing, https://www.msfacess.org/sites/default/files/MSF_assets/HepC/Docs/HepC_brief_OvercomingbarriersToAccess_ENG_2015.pdf.

¹⁸ WHO Fact Sheet <http://www.who.int/mediacentre/factsheets/fs164/en/>, 2016 <http://apps.who.int/iris/bitstream/10665/250625/1/WHO-HIV-2016.20-eng.pdf?ua=1>.

¹⁹ Even Ph. “Le guide de médicaments utiles, inutiles ou dangereux” in *Le Nouvel Observateur*, September 2012, p. 81.

treatment are larger than 90 per cent regardless of the patient's HIV status or prior history of HCV treatment.²⁰

In April 2015, several DAAs were included in the WHO List of Essential Medicines, confirming once more that price is not an obstacle for a medicine to be considered an essential one. At the World Health Assembly in May 2016, WHO member countries approved the Global Health Strategy for Viral Hepatitis for the period 2016-2021.²¹ This strategy aims to eliminate Hepatitis B and C as a public health menace by 2030. Elimination is defined as a 90 per cent reduction in incidence and a 65 per cent reduction in mortality. Achieving these goals implies extending treatment application to 80 per cent of the people living with chronic HBV and HCV diseases.

III.3. Sofosbuvir: Between Financial Engineering and Public Health

According to the quarterly sales reports of Gilead Sciences, historical sales of Sofosbuvir, commercially sold as “Sovaldi & Harvoni”, reached 40 billion US\$ by the first three quarters of 2016. Furthermore, Gilead's 2015 profits reached 18 billion US\$, most of which may be attributed to the company's Hepatitis C medicines. However, despite these massive profits, Gilead did not originally develop Sofosbuvir, as the product was developed by a small American company named “Pharmasset” that Gilead Sciences, realizing the potential of Sofosbuvir, acquired for 11 billion dollars in 2011.²² This means that Gilead Sciences, in its first year of marketing sofosbuvir, fully recovered its investment. Such disproportionate returns—Gilead being but one example of many such cases—questions the justification of the 20 years of patent exclusivity provided by the WTO TRIPS Agreement.

As previously mentioned, in 2014 the American firm Gilead Sciences launched on the market—at a price of 84,000 US\$ for a 12-week treatment—the Hepatitis C medicine known as Sofosbuvir.. A group of British academics²³ estimated that production costs for a twelve-week treatment could reach—in a figure that includes a profit margin of 50 per cent—a price of 62 US\$. Nevertheless, Gilead Sciences has managed to negotiate prices with several governments that reveal large price differences between countries and, above all, prices that have nothing to do with production costs. 50,426 Euros in Germany, 41,680 Euros in France²⁴, 13,000 Euros in Spain, 6,000 Euros in Brazil, 3,465 Euros in Australia.²⁵

Why 41,000 Euros in France and 13,000 Euros in Spain? Everything seems to depend on the negotiation ability of each country. Furthermore, the Gilead's new business model reveals a philosophy of maximizing profits and ignoring any relationship between a medicine's profits and R&D costs. In short, Gilead goes in search of the highest price

²⁰ Pawlotsky JM. “New hepatitis C therapies: the toolbox, strategies, and challenges”, *Gastroenterology* 2014;146(5):1176-92.

²¹ WHO/HIV/2016.06.

²² FOSTER CITY, Calif. & PRINCETON, N.J., “Gilead Sciences to Acquire Pharmasset, Inc. for \$11 Billion”, <http://investors.gilead.com/phoenix.zhtml?c=69964&p=irol-newsArticle&ID=1632335>.

²³ Gotham D, Barber M, Fortunak J, Pozniak A, Hill A. Abstract number A-792-0516-01639, presented at AIDS2016, Durban.

²⁴ On 17th. March, 2017 the French government announced a new reduction to 28,700 Euro for a 12-week treatment; a price which still remains larger than double of what Spain pays. “Soins : le prix des médicaments contre l'hépatite C va baisser”. <http://www.leparisien.fr/laparisienne/sante/soins-le-prix-des-medicaments-contre-l-hepatite-c-va-baisser-31-03-2017-6812619.php>.

²⁵ Price for a 12-week treatment.

governments are willing to pay (even if governments are forced to pay prices that will make universal access impossible, as is the case of France or Spain).

To complete this almost cynical scenario in which a private company seems to be playing with society and governments, on 13 July 2016 the Washington Post published the news that Gilead, using Ireland as a tax haven, has evaded approximately 10 billion dollars of tax payments to the United States Government.²⁶

It is worth remembering that Gilead was the company that sold “Tamiflu” for the H1N1 pandemic, giving exclusive exploitation to the Swiss company Roche. Many countries wasted large sums on precautionary procurement of a medicine that, in the end, scientists ultimately judged to be ineffective. Never in the history of modern medicine had “safety stocks” of such dimensions been made for a medicine whose efficacy was not proven.

III.4. HCV Diagnosis

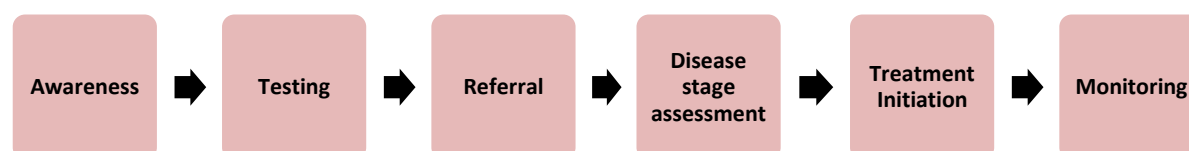
HCV infection is diagnosed in two steps:²⁷

- Detection of anti-HCV antibodies through a serological test revealing the infection.
- In case anti-HCV antibodies are positive, to confirm chronic infection a test detecting the ribonucleic acid (RNA) of the virus is required. As already mentioned about 15 per cent to 45 per cent of infected persons by HCV spontaneously clear the infection by a strong immune response, with no need for treatment.

Once chronic hepatitis C has been diagnosed, the degree of liver damage (fibrosis or cirrhosis) should be assessed. This can be done by liver biopsy or other different non-invasive tests.

Furthermore, a laboratory test to identify the virus genotype should be carried out. Depending on the HCV genotype, treatment should differ. On the other hand, one single person may be infected by more than one genotype.

It is clear that the main barrier to access to treatment for the HCV is currently the price of treatment. Nevertheless, considering that we are dealing with an asymptomatic disease at the beginning, it is important to promote diagnosis, even though it has a certain complexity compared to other diseases with clearer symptoms. We must therefore become conscious of the problem, raise awareness, diagnose, and in many cases, refer the patient to other levels of care, evaluate the stage of the disease, complete the treatment and monitor the patient’s progress. As WHO says, we are dealing with a cascade of steps²⁸:



²⁶ See <http://www.corpwatch.org/article.php/article.php?id=16083>.

²⁷ WHO, Fact sheet, Hepatitis C, 2016. <http://www.who.int/mediacentre/factsheets/fs164/en/>.

²⁸ WHO, “Global report on access to hepatitis C treatment. Focus on overcoming barriers, Geneva, October 2016, available from <http://www.who.int/hepatitis/publications/hep-c-access-report/en/>, p. 9.

“Data is insufficient. Many countries do not understand correctly the true dimension and impact of the hepatitis epidemics from a Public Health perspective. Frequently there is no data at national or sub-national levels or it is insufficient, and surveillance programs are poor, making difficult any planning of specific measures and the establishment of priorities in the assignation of resources.”²⁹

Early diagnosis of viral hepatitis is fundamental for effective treatment and care. According to WHO³⁰, at a global level, less than 5 per cent of persons suffering chronic viral hepatitis know that they are infected. There is a lack of awareness both among the authorities and the general population.

HCV diagnosis is a challenge insofar as it is a process involving two stages. In countries with low resources, access to the test detecting the ribonucleic acid (RNA) of the virus is complex because there are few laboratories equipped to run the test, most of those laboratories are in big cities, and often patients must be referred to a different level of care (which are often in big cities too).³¹

Figures are overwhelming: 95 per cent of people infected with Hepatitis B or C virus are not aware of it. One of the reasons being that it is possible to live for many years without any symptoms, and when infected persons find out they are suffering hepatitis it is often too late for treatment to be fully effective. By then, hepatic damage may have developed into cirrhosis or liver cancer.

It is true that diagnosis of this “silent disease” is an added problem to that of the high cost of treatment, but there are already a good number of lessons learned from various countries that may, if adopted, help accelerate diagnosis and overcome this obstacle.

In a contest organized by WHO and MSF to promote and simplify diagnoses, initiatives have been rather diverse. “Among the initiatives, as well as national testing campaigns, approaches include testing in prisons, testing in the workplace and hospital emergency rooms, integrated HIV-hepatitis testing, as well as the use of Internet, social media, and electronic medical records to flag higher risk patients for testing in primary care.”³²

Experiences range from the realization of tests in Australian prisons to an internet-based risk self-assessment tool in the Netherlands, from community testing camps for drug users in India to testing in primary care facilities in Mongolia. In the Netherlands, thousands of red covers for bicycle seats were distributed with inscriptions targeting increased awareness of the need for hepatitis C testing.

The contest organized by WHO and MSF served to demonstrate a wide range of possibilities and showed that if we can develop initiatives for HCV diagnosis that suit

²⁹ WHO, Global health sector strategy on viral hepatitis 2016–2021: Towards ending viral hepatitis, p. 14.

³⁰ WHO, Global health sector strategy on viral hepatitis 2016–2021: Towards ending viral hepatitis. <http://apps.who.int/iris/bitstream/10665/246178/1/WHO-HIV-2016.05-eng.pdf>, p. 36.

³¹ WHO, “Global report on access to hepatitis C treatment. Focus on overcoming barriers, Geneva, October 2016, p. 10.

³² WHO, <http://www.who.int/features/2016/access-hepatitis-testing/en/>.

different settings and cultures, then we will be able to increase effective hepatitis diagnosis in a greater number of countries and communities.³³

III.5. World Health Organization Standardized Treatment Guidelines

Recognizing the serious public health problem of HCV and the great promise represented by the new DAAs treatments, WHO developed in 2014³⁴ the first guidelines of standardized treatments. These guidelines were already reviewed in 2016 due to the fast evolution of treatments for the different genotypes. A new review is scheduled for 2017.³⁵

III.6. The Sofosbuvir Patents

It is important to keep in mind that when talking of patents for pharmaceutical products we are talking of patents of diverse types, as for example³⁶:

Product patents: claiming a chemic molecule / active pharmaceutical ingredient

Process patents: protecting the manufacture of a certain product.

There are also many other types of patents, unaccepted by many countries as Argentina, Brazil or India, but among which we find hundreds and thousands of the current patents of pharmacological products, such as:

Formulation patents: of the dosage form, as, for example, on tablets of delayed release of the active ingredient.

Combination patents: claiming the combination of two or more existing active ingredients.

Patents on salts, ethers and esters: solid forms obtained by routine methods.

Patents of polymorphic forms: a polymorph is an intrinsic property of chemical products; polymorphs are not invented; instead they are only discovered and therefore should not be patented.

Patents including a “Markush” claim: very broad claims covering chemical structures that may include a family of thousands or millions of compounds.

Selection patents: claiming only a single element or segment of a Markush patent, for example, which was already included in the patented item.

Patents on analogy processes: covering an obvious method to produce a new compound.

³³ Ibid.

³⁴ WHO, Guidelines for the screening, care and treatment of persons with hepatitis C infection. <http://www.who.int/hiv/pub/hepatitis/hepatitis-c-guidelines/en/>.

³⁵ WHO, “Global report on access to hepatitis C treatment. Focus on overcoming barriers, Geneva, October 2016, p. 22.

³⁶ Carlos Correa, “Guidelines for Pharmaceutical Patent Examination: Examining Pharmaceutical Patents from a Public Health Perspective”. WHO, ICTSD, PNUD, UNCTACD, Geneva, 2008.

Patents on active metabolites and prodrugs: metabolites are produced by the organism and cannot be considered an invented product. Prodrugs are inactive compounds that transform inside the organism into the therapeutically active principle, with which it shares the same active part of a molecule.

Patents on treatment methods: including prevention, diagnosis or prophylaxis methods; they do not protect a product itself but the way in which the product is used and, therefore, may not be patented since they lack a key patenting requirements: namely industrial application.

Patents on second uses: second uses or second indications of a product, over which there are already a great number of patents, should not be patentable as this is not a case of invention but of a discovery, which, in most cases, happens through medical practice and not in research laboratories of the pharmaceutical industries.

In the particular case of Sofosbuvir, a study conducted by WHO³⁷ revealed that this product is covered by 21 different types of patents: 2 Markush type patents that could give rise to dozens more, 4 process patents, 9 patents on salts and polymorphs, one patent on the combination of two products, and 3 patents on method of usage: “substance for the HCV treatment.”

Several of these Sofosbuvir patents are now the subject of litigation or oppositions in different countries, showing the fragility and lack of evidence that it should be considered a true genuine innovation. (Cf. 3.7.)

III.7. Oppositions to the Sofosbuvir Patent of Gilead

The Non-Governmental Organizations I-MAK (Initiative for Medicines, Access & Knowledge) and the Delhi Network of Positive People (DNP+) presented an opposition to Gilead’s Sofosbuvir patent application in India. The lawyers of these two organizations claim that the medicine represents “old science” and therefore does not meet the patentability standards of India.³⁸

Sofosbuvir patents have been rejected in Egypt, China and Ukraine and have met oppositions in Argentina, Brazil, Russia, Thailand and the European Union.³⁹

Two of the challenged cases in India make reference to the crystalline form of sofosbuvir and daclatasvir that, in accordance to the Indian Patent Law, are not patentable unless evidencing a significant increase in therapeutic effect. There is a third opposition against velpatasvir (which combined with sofosbuvir is sold by Gilead under the brand name of “Epclusa”) because it is considered as an obvious modification of the structure of a

³⁷ WHO, Patent situation of key products for treatment of hepatitis C: Sofosbuvir, Geneva, March 2015.

³⁸ MSF “Access: Patent challenge hearing on Gilead hepatitis C drug sofosbuvir starts in India”, <http://www.msf.org/en/article/access-patent-challenge-hearing-gilead-hepatitis-c-drug-sofosbuvir-starts-india>.

³⁹ Ibid.

previous medicine for Hepatitis C “ledipasvir” (which combined with sofosbuvir is sold by Gilead under the brand name of Harvoni).⁴⁰

A copy of the patent oppositions can be found with the following links:

<https://www.patentoppositions.org/en/drugs/daclatasvir>

<https://www.patentoppositions.org/en/drugs/sofosbuvir>

<https://www.patentoppositions.org/en/drugs/velpatasvir>

III.8. Voluntary Licenses Granted by Gilead

“In November 2013 and February 2014, public interest groups and generics companies filed the first patent oppositions against Gilead Sciences (Gilead)’s patent applications in India. Within months, Gilead signed voluntary license agreements with eleven Indian generics pharmaceutical companies and API manufacturers for the HCV DAAs sofosbuvir, ledipasvir and velpatasvir”.⁴¹

In 2014, Gilead issued voluntary licenses to 11 Indian manufacturers of medicine generics, giving them the possibility to market the product to a restricted list of 101 countries.⁴² The prices of these Indian generic versions represent an important progress. (From September 2016 Sofosbuvir “under the Gilead license” costs 750 US dollars and the other two medicines, Harvoni and Epclusa, cost 900 US dollars per treatment⁴³, instead of the 84,000 US dollars price in the United States.) However, its access is not allowed to the poorer countries of the restricting list⁴⁴. In the other 94 countries excluded from the Gilead list, treatments are far from being accessible, and such rationing applies to many of the world’s richest countries, including ones from Europe and North America.

Negotiations for the introduction of voluntary licenses between the patent holder and another actor in a given country, or operating in that country’s market, may contribute to the reduction of prices. The benefits of voluntary licensing agreements depend largely on the conditions of the license itself.

Patent holders may, at their own discretion, issue to the other parties, with exclusive character or not, the rights to produce, import and/or distribute a pharmaceutical product. Depending on the terms of the license, the licensee may act completely or effectively as a representative of the patent holder, or be free to establish the conditions of sale and distribution of the product in a certain market or markets, in exchange for the payment of a royalty. Either of these options, or even intermediate agreements, can lead to a considerable

⁴⁰ MSF, “Flawed patents on hepatitis C drugs latest to be challenged in global push for access” February 2017. <https://msfaccess.org/about-us/media-room/press-releases/flawed-patents-hepatitis-c-drugs-latest-be-challenged-global-push>.

⁴¹ MSF Access Campaign, “Access to Sofosbuvir, Ledipasvir and Velpatasvir analysis & key recommendations on Gilead voluntary licence, March 2015.

⁴² MSF Briefing Document, https://www.msfast.org/sites/default/files/MSF_assets/HepC/Docs/HepC_brief_OvercomingbarriersToAccess_ENG_2015.pdf.

⁴³ <http://www.gilead.com/~media/files/pdfs/other/chronic%20hepatitis%20c%20medicines%20pricing%20-%20september%202016.pdf>.

⁴⁴ Access to the generics made under Indian voluntary licenses is restricted only to the poorer countries that comprise the license territory.

reduction in prices. Nevertheless, the terms of a voluntary license may establish price margins or include clauses to keep prices at a similar price to that offered by the patent holder. At times, export possibilities are limited, or anti-diversion measures are required, as is the case with Gilead and the 11 licenses granted to manufacturers in India. Again, such issues will depend on the conditions of the license agreement, and such contracts are often confidential.

Voluntary licensing agreements, at the discretion of the patent holder, take place in general for strategic commercial reasons (as for example to penetrate a market) rather than as a mechanism to ensure access to the largest number of people.⁴⁵

MSF expressed worries concerning the voluntary licenses granted by Gilead in India, and these worries can be summarized as follows:⁴⁶

- Gilead licensing obligations and restrictions can undermine access and exclude millions of patients with HCV.
- There are approximately 49 million people living with HCV in developing countries excluded by this license.
- Gilead's license for DAAs lack transparency, and can be translated as an "evergreening" strategy.
- Gilead has provided no information on the type of applications being submitted in the excluded countries. Gilead has applied for secondary patents (crystallization forms, compositions, etc.) that, although weak and easy to reject in principle, will block competition from generic medicines in the countries where they are accepted.
- The definition of patents in voluntary licenses is too broad, (includes patents and patent applications), and refers to both primary and secondary patents as treatment method patents. This fact leads to a certain ambiguity, as for instance whether it would be possible to export or not to a country excluded from the Gilead licenses but issuing a compulsory license.
- Gilead has negotiated its voluntary licenses both for the end product and for the raw material (APIs) only with India but not with China or Brazil for example, and this is problematic in terms of the expansion of a global market of generics.
- Gilead has segmented the APIs market by means of the following strategies: firms licensed by Gilead may only obtain APIs through other licensees from India or from other Gilead suppliers, with its prior approval.
- Gilead does not authorize its licensees to import from potential Chinese manufacturers who would be able to produce much cheaper APIs and other intermediate substances.

III.9. Anti-diversion Measures

Pharmaceutical companies have imposed what they call anti-diversion measures that both public programs and private dealers have to comply with. The argument used to justify these measures is that developing countries have much cheaper products that may be re-exported to

⁴⁵ Velasquez, G., Correa C., Weisman R. "Cost-containment mechanisms for essential medicines, including antiretrovirals, in China" Health Economics and Drugs EDM Series No. 13, WHO/EDM/PAR/2003.6.

⁴⁶ Ibid.

developed countries. To this end, the industry is making use of a large list of measures, many of which are not ethically justifiable since they violate patient confidentiality.

A simple modification of packaging, or different brand names, or even a change in the colour of capsules or tablets would be enough. Much has been debated on electronic product tracking, a measure that would unnecessarily increase the cost of products, but there are other industry practices that go against patient confidentiality and should be simply rejected.

The measures required in the voluntary licenses granted by Gilead not only violate the rights of patients but also place a burden on health systems and providers of medicines.⁴⁷

According to WHO,⁴⁸ reported anti-diversion practices include:

- Distribution of medicines with bar codes including information on the patients;
- Access to medicines being made contingent on the name of the patient and requiring identification;
- Demanding a proof of place of residence and nationality to deliver the medicines;
- Taking photographs of patients when delivering the medicines;
- Incomplete distribution of treatment requiring patients to return and show the first or most recent (empty) bottle;
- Require a negative viral load test if patients have lost the package.

This type of measure, in addition to violating patients' confidentiality rights, hinders the expansion of treatment and penalizes vulnerable populations such as peasants, migrants, prisoners or homeless people.

Human rights violations, along with widespread stigma and discrimination, continue to hinder access to health services for populations that may be marginalized and perhaps criminalized and who are at higher risk of hepatitis infection.⁴⁹

⁴⁷ Ibid.

⁴⁸ WHO, "Global report on access to hepatitis C treatment. Focus on overcoming barriers", Geneva, October 2016, p. 33.

⁴⁹ WHO, Global Health Sector strategy on viral Hepatitis 2016-2021: Towards ending viral hepatitis. <http://apps.who.int/iris/bitstream/10665/246177/1/WHO-HIV-2016.06-eng.pdf>, p. 14.

IV. HOW TO OVERCOME THE BARRIERS TO ACCESS USING TRIPS FLEXIBILITIES

The voluntary license granted by Gilead to 11 generic manufacturers of India excludes, besides all developed countries, 41 middle-income countries.

Middle-income countries excluded from the voluntary license of Gilead⁵⁰

Albania	Costa Rica	Kosovo	Saint Lucia
Argentina	Dominican Republic	Lebanon	Syria
Armenia	Ecuador	Macedonia	Thailand
Azerbaijan	Georgia	Malaysia	Turkey
Belarus	Grenada	Mexico	Ukraine
Belize	Hungary	Moldova	Venezuela
Bosnia and Herzegovina	Iran	Montenegro	West Bank and Gaza
Brazil	Iraq	Panama	Yemen
Bulgaria	Jamaica	Peru	
China	Jordan	Romania	
Colombia	Kazakhstan	Serbia	

All countries excluded from the voluntary license of Gilead (or other companies arriving to similar agreements) do have legal options on which to lean to ensure supply of DAAs or any other essential medicine protected by a patent at inaccessible prices. Below we enumerate the different strategies and measures that countries can adopt to ensure universal access to the DAAs treatments.

IV.1. Information on International Prices

Gilead Sciences has opted for a pricing strategy that reflects the negotiation capabilities of each country. Differences may be significant even between countries of similar economic and social development. 13,000 Euro for a 12-week treatment in Spain against 41,000 Euro for the same treatment in France or 900 dollars in Egypt against the 51,000 US\$ in Argentina.

Care must be taken during negotiation with the originating companies about the conditions eventually included in the contracts, such as renouncing to use some flexibilities of the TRIPS Agreement, or waiving parallel imports, or admitting import restrictions of raw material.

It is also advisable to know the prices of generics in the countries where the DAAs have not being patented, in order to evaluate whether it is needed or not to issue a compulsory license to ensure universal access.

⁵⁰ MSF briefing, version of November , 2016:

https://www.msfaaccess.org/sites/default/files/MSF_assets/HepC/Docs/HepC_statement_AnalysisOfGileadLicense_ENG_2015.pdf.

IV.2. Adoption of Patentability Criteria from a Public Health Perspective⁵¹

It is important to remember that a patent is a territorial right and that it is therefore possible that a patent is granted for an invention in one country but that the very same patent application could be legally rejected by another country. At the same time, a patent that has been issued in one country can be revoked if it is demonstrated that the patent office should not to have granted it.

It is also important to highlight that in the pharmaceutical sphere, the situation is not ONE product, ONE patent. An invention can be protected by numerous patents, just as the production process for the product can also be protected by one or numerous patents; therefore, in many countries there exist several types of patents that are applied to a single pharmaceutical product. (According to the previously mentioned WHO study⁵², Sofosbuvir is the subject of 21 types of patents, Cf. 3.6). As a result, a single medicine can be protected by a large number of patents.

In principle, the patent system was conceived to ensure that the public benefited from inventions. Currently, a large number of people living in developing countries not only do not benefit from inventions but, in many countries, patents represent a barrier to access to life-saving medicines. These obstacles to life-saving medicine exist simply because business logic prevails over the right to health care access.

The patentability requirements used by national intellectual property offices, according to the TRIPS Agreement, require a product or manufacturing process to meet the conditions necessary to grant patent protection, namely: novelty, inventive step and industrial applicability (utility). These three elements, however, are not defined in the TRIPS Agreement and WTO Member States are free to define these three criteria in a manner consistent with the public health objectives defined by each country.

According to the report of the United Nations High Commissioner for Human Rights “the requirements under the TRIPS Agreement for the grant of patents – novelty, inventive step and industrial applicability – are open to interpretation under national legislation and each country can decide according to local conditions. Consequently, the High Commissioner encourages interpretations of these requirements that do not lose sight of the public interest in the wide dissemination of knowledge...”⁵³

The fact that the TRIPS Agreement does not define novelty, inventive step and industrial applicability (utility) leaves countries significant room for manoeuvre; therefore patentability requirements represent the principal and most important flexibility allowed by the Agreement to protect public health and access to medicines. “Politicians and legislators have broad room for manoeuvre to give legal effect to those flexibilities”.⁵⁴

⁵¹ Velasquez, G. “Guidelines on Patentability and Access to Medicines”, *Research Paper* 61, South Centre, March, 2015.

⁵² WHO, Patent situation of key products for treatment of hepatitis C: Sofosbuvir, Geneva, March 2015.

⁵³ The impact of the Agreement on Trade-Related Aspects of Intellectual Property Rights on human rights: Report of the High Commissioner, E/CN.4/Sub.2/2001/13, 27 June 2001, paragraph 62.

⁵⁴ Arias, Eduardo, PPT on “Pautas para el examen de patentabilidad de invenciones químico-farmacéuticas, INPI, Argentina, 2014.

IV.3. Compulsory Licenses – Aspects and Practical Procedures⁵⁵

Article 31 of the WTO TRIPS Agreement explicitly allows the granting of compulsory licenses. The Agreement contains no limits on the grounds under which such licenses can be granted. Members' right to determine such grounds has been confirmed by the Doha Declaration on the TRIPS Agreement and Public Health (November 2001).

Article 31 makes particular, but not exhaustive, reference to cases of national emergency or extreme urgency, dependency of patents, licenses for governmental non-commercial use, and licenses to remedy anti-competitive practices. National laws can, however, provide for the granting of such licenses whenever the titleholder refuses to grant a voluntary license "on reasonable commercial terms" (Article 31 (b)) and for other reasons, such as public health or broad considerations of public interest. The Agreement permits that compulsory licenses provide licensees the authority to exercise any of the rights conferred by a patent, including production or importation.

The granting of a compulsory license within the framework of national legislation (and in conformity with the TRIPS Agreement) requires a body of measures described here below.

IV.3.1. *Identify relevant patents*

It is often a true challenge for ministries of health to identify all primary and secondary patents around a given product. Historically, patent offices and health ministries have not developed strong links between them; however, countries such as Argentina, Brazil, Thailand, Ecuador or India have started to establish such links in order to make effective use of the flexibilities of the TRIPS Agreement, notably the granting of compulsory licenses. In 2015, WHO published – with the promise to keep it updated – a study of the landscape of the patents related to Hepatitis C, a very useful tool for countries wishing to issue a compulsory license or to make parallel imports. There is also a database, developed by the MPP, with the landscape of HCV patents.⁵⁶

In most cases, pharmaceutical products are protected by a patent for the active ingredient (primary patent) and by different (secondary) patents for formulations, production processes, new indications, etc. All these patents must be identified and included in the compulsory license, as appropriate, in order to be able to ensure the autonomy to develop the necessary product. Otherwise, the use of the invention targeted by the compulsory license may be disturbed or blocked by allegations of infringement of the secondary patents (as exemplified by the well documented case of the DDI product in Thailand).

IV.3.2. *Explore possible sources of supply based on local production*

The analysis to be undertaken should include:

- the availability of technical resources for reverse engineering;
- the cost and duration of developing manufacturing processes and formulations;

⁵⁵ This point on the aspects and practical procedures for the granting of a Compulsory License is based on the article by Velasquez G., Correa C., Weisman R. "Cost-containment mechanisms for essential medicines, including antiretrovirals, in China", Health Economics and Drugs EDM Series No. 13, WHO/EDM/PAR/2003.6

⁵⁶ See <http://www.medicinespatentpool.org/patent-data/patent-status-of-arvs/>.

- the need for technology transfer;
- GMP and quality of final products made by local producers; and
- estimates of the investment required and of the marginal cost of production.

IV.3.3. Identify possible sources of importation of the required medicines

The analysis to be undertaken should include:

- compliance with GMP and product quality assurance by potential suppliers;
- prices of supply over time; and
- the sustainability of the exporter's supply.

IV.3.4. Marketing approval

Registration requirements may represent an obstacle to rapid distribution of the necessary medicines, as could happen, for example, when the country has introduced a period of exclusivity for the protection of data coming from tests. When examining the possibility of issuing a compulsory license, all necessary measures should be taken to ensure that these obstacles will not be present or may be overcome.

IV.3.5. Request for a compulsory license

The applicable conditions will depend on the alternatives and modalities chosen by each country according to its national legislation.

A request to the patent holder on reasonable commercial terms should be made, including:

- information about the requesting party;
- the expected volume of production;
- the royalty to be paid;
- the form of payment;
- the intended mode of use of the invention;
- quality controls;
- trademark to be used, if any;
- the duration of the license;
- the licensee's right to control sales for determination of royalties due;
- the applicable law and jurisdiction in case of disputes.

Some laws and regulations do not delimit a "reasonable period of time" for the patentee to accept or reject the offer, but a period of one to three months may be considered reasonable.

When dealing with governmental use, no prior negotiations are required; "public interest" constitutes a legitimate reason to grant a compulsory license.

Declaring a "national emergency" is not a requirement for a compulsory license to be granted. When choosing this option, it should be borne in mind that an "emergency" can be a long-term situation, as it happens with the HIV/AIDS pandemic, and not just a short-term problem.

In many cases a compulsory license for government use is preferable both because no prior negotiations are required and also because it will be clear from the start that the government's basic criterion for granting a compulsory license is public health. In this way, it is politically more difficult for patent holders, their trade associations and their respective governments to question the compulsory license.

IV.3.6. Granting of the compulsory license by the competent department

The competent department will have to define the scope of the license and its duration. It would be advisable for the scope to include all commercial and non-commercial uses of the relevant invention, and for the license to last until the patents' expiry.

IV.3.7. Negotiation with patent holder about royalty rate

After the granting of the compulsory license, bona fide negotiations should be undertaken with the patent holder to establish the royalty rate for the exploitation of the patent. Generally, these royalties are determined as a percentage of the net sales price of the generic product made under the license (and not the patentee's own product), but other modalities can be adopted, for instance, a fixed sum per unit sold.

The TRIPS Agreement requires that the compensation reflect the economic value of the license.

Commercial practice in voluntary licensing is to use royalties ranging between 2 per cent and 5 per cent, though they may be higher in certain cases. There is some evidence available on the royalties determined by national authorities in Canada, the USA, and other countries for the granting of compulsory licenses.⁵⁷

Factors that may be considered to negotiate the royalties include: launch date of the product; possible substitutes; coverage and possible invalidity (total or partial) of the patent(s); pending challenges to the patent(s), if any; accumulated sales and recovery of R&D investment made by the patent holder; global market for the product (units and value); expected volume of production and price under the compulsory license; and royalties agreed upon in voluntary licenses on the same or similar products.

Of course, gathering this information will require considerable preparation and work by an inter-disciplinary team.

IV.3.8. Determination of royalty fee by the Patent Administration Department

If the negotiations on the royalty fee fail, it will be set by the Patent Administration Department or the corresponding body charged with the relevant authority by law. For the sake of transparency and consistency, it would be advisable to make explicit the criteria used for this purpose and to design guidelines applicable to all such determinations of royalty fees.

⁵⁷ Niess, P. "Technology evaluation and pricing". Tech Monitor, November-December 1999, pp. 16-17.

IV.3.9. Appeal

National legislations establish the modalities by which patent holders may file an appeal against a decision to grant a compulsory license; it is important that the appeal does not suspend the execution of the aforementioned compulsory license.

IV.3.10. Other considerations

Patent holders (or their governments) may attempt to use legal measures, such as injunctions, to delay or prevent the execution of a compulsory license. It would also be useful to check for the possible application of other instruments, such as bilateral agreements on investment (or BITs), which often consider intellectual property as an "asset" subject to their rules.

V. SOME COUNTRIES HAVE LAUNCHED THE NEW HCV TREATMENT

In several countries the role of civil society organizations has been, and still remains, fundamental for the government to initiate diagnosis and treatment campaigns. In **Australia**, for example, in December 2015 the government announced an investment of more than 1 billion US dollars to enable universal access to HCV treatment. According to the statement from the Australian Government,⁵⁸ an estimated 230,000 Australians are living with HCV, and these people would have access to DAA treatment through the State Pharmaceutical Benefit Scheme (PBC).

In **France**, it is estimated that 500,000 people live with HCV; however, only 30,000 persons are currently (2016) following the DAAS treatment because the price negotiated with Gilead is approximately of 40,000 Euros for a twelve-week treatment. At this price, some observers wonder whether Minister Marisol Touraine's announcement of universal access to HCV treatment is possible.⁵⁹ The humanitarian organization “Médecins du Monde” has demanded that the government to issue a compulsory license to allow universal access to the treatment.⁶⁰

In **Egypt**, the country with the highest rate of HCV infection in the world, the government managed to negotiate with Gilead a 12- week treatment price of 900 US dollars. Following the announcement of this discount, the United States Senate addressed a letter to John Martin, President of the Gilead⁶¹ and began an investigation into the reasons for the price differential of 900 US dollars in Egypt and the 84,000 US dollars in the US. In practice, the price of treatment is often higher (double), as patients with advanced HCV often need a 24-week treatment.

The Egyptian National Patent Office, applying more strict patent criteria than many other countries, rejected one of the Sofosbuvir patent applications, allowing the Egyptian firm “Pharco” to produce for less than 200 US\$ per 12-week treatment.

In 2015 alone, 170,000 people received treatment in Egypt and in 2016 more than 500,000 started DAAs treatment. More than 90 per cent of the HCV patients in this country are infected with genotype 4, something that simplifies treatment protocols.⁶²

In **Morocco** the original patents on Sofosbuvir, Ledipasvir and Daclatasvir were never requested, and this has allowed importation and local production of generics. In Morocco as in other countries, civil society groups such as ITPC (International Treatment Preparedness

⁵⁸ [http://www.health.gov.au/internet/ministers/publishing.nsf/Content/FAE2B65331456243CA257F20006D4C48/\\$File/SL-154.pdf](http://www.health.gov.au/internet/ministers/publishing.nsf/Content/FAE2B65331456243CA257F20006D4C48/$File/SL-154.pdf).

⁵⁹ Vaugrente A. “Accès aux nouveaux traitements Hépatite C : l’annonce de Marisol Touraine saluée mais surveillée”: <http://www.pourquoidoctor.fr/Articles/Question-d-actu/15845-Hepatitis-C-l-annonce-de-Marisol-Touraine-saluee-mais-surveillee>.

⁶⁰ Médecins du Monde. https://issuu.com/medecinsdumonde/docs/mdm_hep_c_brevet_web.

⁶¹ Letter of the Senate of the United States to the CEO of Gilead Sciences: <https://www.finance.senate.gov/imo/media/doc/Wyden-Grassley%20Document%20Request%20to%20Gilead%207-11-141.pdf>

⁶² Plan of action for the prevention, care and treatment of viral hepatitis, Egypt 2014-2018. Ministry of Health and Population. http://www.emro.who.int/images/stories/egypt/VH_Plan_of_Action_FINAL_PRINT1.pdf.

Coalition) have played an important role on the path leading to the government's announcement of expanding treatment measures.

The cost of a twelve-week treatment with the generic Sofosbuvir, marketed as "SSB", is approximately 9,000 Dirhams (approximately 900 US dollars). The Health Ministry announced that Morocco will be free of Hepatitis C by 2030.⁶³

Pakistan is a country with a high prevalence of HCV. Primary patents for Sofosbuvir were not filed and requests on some secondary patents are still pending. According to a survey conducted by WHO, the price for a twelve-week treatment with locally-manufactured generic Sofosbuvir is the cheapest in the world, at 45 US dollars per twelve-week treatment.⁶⁴

In Thailand, following progress in antiviral access achieved by groups of patients living with HIV, the Treatment Action Group (TAG) has developed campaigns to raise awareness both on the government and the public opinion in order to accelerate programs of treatment access to Hepatitis C.

The non-governmental organization TAG filed with the patent office an opposition to the patent application for the Sofosbuvir by Gilead.⁶⁵

⁶³ Morocco World News: <https://www.moroccoworldnews.com/2015/11/173627/morocco-without-hepatitis-c-in-2020/>.

⁶⁴ WHO, "Global report on access to hepatitis C treatment. Focus on overcoming barriers, Geneva, October 2016, p. 30.

⁶⁵ TAG, "Gilead: Stop Blocking Access to Hepatitis C Treatment" <http://www.treatmentactiongroup.org/hcv/2015/gilead-stop-blocking-HCV-access>.

CONCLUSIONS

- The eradication of the disease is only possible if medicines can be purchased at low prices within health budgets.
- New ways of delivering mass treatment programs for Hepatitis C are needed.
- It is necessary to become conscious of the problem, raise awareness, diagnose and, in many cases, refer the patient to another level of care, evaluate the stage of the disease, follow the treatment and monitor the patient's progress.
- Most medicines have low production costs; pharmaceutical companies could make high levels of profit if they would decide to sell large quantities at reasonable prices.

If pharmaceutical companies refuse to lower prices, it would be necessary to consider:

- Compulsory licenses.
- Parallel imports.
- Use of the money coming from their tax evasion to pay for treatments.
- Promotion of the manufacture of generics.
- Summoning them before Justice for a violation of Human Rights.

20 Years of “R”evolution			
1996		2016	
1.	27,000 patients with ARVs	1.	15-17 million, currently
2.	Treatment cost: 12,000 US\$	2.	Cost: Less than 100 US\$
3.	WHO, HM and some NGOs	3.	The Whole UN, Ministries, NGOs
4.	NDP: a question of health	4.	NDP: Health, Trade, Human Rights, IP
5.	A2M= political will or charity	5.	A2M = A question of Rights
6.	CL for medicines = 0	6.	More than 30 CL in 11 countries
7.	R&D – IP model: ACCEPTED	7.	R&D model: QUESTIONED
8.	Patients were patient	8.	Patients are impatient
9.	Pharmaceutical Industry: impunity	9.	Phar. Ind. = Held accountable
10.	Price of ARV 100 times its cost	10.	Hepatitis C price: 1,400 times its cost

SOUTH CENTRE RESEARCH PAPERS

No.	Date	Title	Author
1	November 2005	Overview of the Sanitary and Phytosanitary Measures in QUAD Countries on Tropical Fruits and Vegetables Imported from Developing Countries	Ellen Pay
2	November 2005	Remunerating Commodity Producers in Developing Countries: Regulating Concentration in Commodity Markets	Samuel G. Asfaha
3	November 2005	Supply-Side Measures for Raising Low Farm-gate Prices of Tropical Beverage Commodities	Peter Robbins
4	November 2005	The Potential Impacts of Nano-Scale Technologies on Commodity Markets: The Implications for Commodity Dependent Developing Countries	ETC Group
5	March 2006	Rethinking Policy Options for Export Earnings	Jayant Parimal
6	April 2006	Considering Gender and the WTO Services Negotiations	Meg Jones
7	July 2006	Reinventing UNCTAD	Boutros Boutros-Ghali
8	August 2006	IP Rights Under Investment Agreements: The TRIPS-plus Implications for Enforcement and Protection of Public Interest	Ermias Tekeste Biadgleng
9	January 2007	A Development Analysis of the Proposed WIPO Treaty on the Protection of Broadcasting and Cablecasting Organizations	Viviana Munoz Tellez and Andrew Chege Waitara
10	November 2006	Market Power, Price Formation and Primary Commodities	Thomas Lines
11	March 2007	Development at Crossroads: The Economic Partnership Agreement Negotiations with Eastern and Southern African Countries on Trade in Services	Clare Akamanzi
12	June 2007	Changes in the Governance of Global Value Chains of Fresh Fruits and Vegetables: Opportunities and Challenges for Producers in Sub-Saharan Africa	Temu A.E and N.W Marwa
13	August 2007	Towards a Digital Agenda for Developing Countries	Dalindyebo Shabalala
14	December 2007	Analysis of the Role of South-South Cooperation to Promote Governance on Intellectual Property Rights and Development	Ermias Tekeste Biadgleng
15	January 2008	The Changing Structure and Governance of Intellectual Property Enforcement	Ermias Tekeste Biadgleng and Viviana Munoz Tellez
16	January 2008	Liberalization of Trade in Health Services:	Joy Kategekwa

		Balancing Mode 4 Interests with Obligations to Provide Universal Access to Basic Services	
17	July 2008	Unity in Diversity: Governance Adaptation in Multilateral Trade Institutions Through South-South Coalition-Building	Vicente Paolo B. Yu III
18	December 2008	Patent Counts as Indicators of the Geography of Innovation Activities: Problems and Perspectives	Xuan Li
19	December 2008	WCO SECURE: Lessons Learnt from the Abortion of the TRIPS-plus-plus IP Enforcement Initiative	Xuan Li
20	May 2009	Industrialisation and Industrial Policy in Africa: Is it a Policy Priority?	Darlan F. Marti and Ivan Ssenkubuge
21	June 2009	IPR Misuse: The Core Issue in Standards and Patents	Xuan Li and Baisheng An
22	July 2009	Policy Space for Domestic Public Interest Measures Under TRIPS	Henning Grosse Ruse – Khan
23	June 2009	Developing Biotechnology Innovations Through Traditional Knowledge	Sufian Jusoh
24	May 2009	Policy Response to the Global Financial Crisis: Key Issues for Developing Countries	Yılmaz Akyüz
25	October 2009	The Gap Between Commitments and Implementation: Assessing the Compliance by Annex I Parties with their Commitments Under the UNFCCC and its Kyoto Protocol	Vicente Paolo Yu III
26	April 2010	Global Economic Prospects: The Recession May Be Over But Where Next?	Yılmaz Akyüz
27	April 2010	Export Dependence and Sustainability of Growth in China and the East Asian Production Network	Yılmaz Akyüz
28	May 2010	The Impact of the Global Economic Crisis on Industrial Development of Least Developed Countries	Report Prepared by the South Centre
29	May 2010	The Climate and Trade Relation: Some Issues	Martin Khor
30	May 2010	Analysis of the Doha Negotiations and the Functioning of the World Trade Organization	Martin Khor
31	July 2010	Legal Analysis of Services and Investment in the CARIFORUM-EC EPA: Lessons for Other Developing Countries	Jane Kelsey
32	November 2010	Why the IMF and the International Monetary System Need More than Cosmetic Reform	Yılmaz Akyüz
33	November 2010	The Equitable Sharing of Atmospheric and Development Space: Some Critical Aspects	Martin Khor
34	November 2010	Addressing Climate Change through Sustainable Development and the Promotion of Human Rights	Margreet Wewerinke and Vicente Paolo Yu III

35	January 2011	The Right to Health and Medicines: The Case of Recent Negotiations on the Global Strategy on Public Health, Innovation and Intellectual Property	Germán Velásquez
36	March 2011	The Nagoya Protocol on Access and Benefit Sharing of Genetic Resources: Analysis and Implementation Options for Developing Countries	Gurdial Singh Nijar
37	March 2011	Capital Flows to Developing Countries in a Historical Perspective: Will the Current Boom End with a Bust?	Yılmaz Akyüz
38	May 2011	The MDGs Beyond 2015	Deepak Nayyar
39	May 2011	Operationalizing the UNFCCC Finance Mechanism	Matthew Stilwell
40	July 2011	Risks and Uses of the Green Economy Concept in the Context of Sustainable Development, Poverty and Equity	Martin Khor
41	September 2011	Pharmaceutical Innovation, Incremental Patenting and Compulsory Licensing	Carlos M. Correa
42	December 2011	Rethinking Global Health: A Binding Convention for R&D for Pharmaceutical Products	Germán Velásquez and Xavier Seuba
43	March 2012	Mechanisms for International Cooperation in Research and Development: Lessons for the Context of Climate Change	Carlos M. Correa
44	March 2012	The Staggering Rise of the South?	Yılmaz Akyüz
45	April 2012	Climate Change, Technology and Intellectual Property Rights: Context and Recent Negotiations	Martin Khor
46	July 2012	Asian Initiatives at Monetary and Financial Integration: A Critical Review	Mah-Hui (Michael) Lim and Joseph Anthony Y. Lim
47	May 2013	Access to Medicines and Intellectual Property: The Contribution of the World Health Organization	Germán Velásquez
48	June 2013	Waving or Drowning: Developing Countries After the Financial Crisis	Yılmaz Akyüz
49	January 2014	Public-Private Partnerships in Global Health: Putting Business Before Health?	Germán Velásquez
50	February 2014	Crisis Mismanagement in the United States and Europe: Impact on Developing Countries and Longer-term Consequences	Yılmaz Akyüz
51	July 2014	Obstacles to Development in the Global Economic System	Manuel F. Montes
52	August 2014	Tackling the Proliferation of Patents: How to Avoid Undue Limitations to Competition and the Public Domain	Carlos M. Correa
53	September 2014	Regional Pooled Procurement of Medicines in the East African Community	Nirmalya Syam
54	September 2014	Innovative Financing Mechanisms:	Deborah Ko Sy, Nirmalya

		Potential Sources of Financing the WHO Tobacco Convention	Syam and Germán Velásquez
55	October 2014	Patent Protection for Plants: Legal Options for Developing Countries	Carlos M. Correa
56	November 2014	The African Regional Intellectual Property Organization (ARIPO) Protocol on Patents: Implications for Access to Medicines	Sangeeta Shashikant
57	November 2014	Globalization, Export-Led Growth and Inequality: The East Asian Story	Mah-Hui Lim
58	November 2014	Patent Examination and Legal Fictions: How Rights Are Created on Feet of Clay	Carlos M. Correa
59	December 2014	Transition Period for TRIPS Implementation for LDCs: Implications for Local Production of Medicines in the East African Community	Nirmalya Syam
60	January 2015	Internationalization of Finance and Changing Vulnerabilities in Emerging and Developing Economies	Yılmaz Akyüz
61	March 2015	Guidelines on Patentability and Access to Medicines	Germán Velásquez
62	September 2015	Intellectual Property in the Trans-Pacific Partnership: Increasing the Barriers for the Access to Affordable Medicines	Carlos M. Correa
63	October 2015	Foreign Direct Investment, Investment Agreements and Economic Development: Myths and Realities	Yılmaz Akyüz
64	February 2016	Implementing Pro-Competitive Criteria for the Examination of Pharmaceutical Patents	Carlos M. Correa
65	February 2016	The Rise of Investor-State Dispute Settlement in the Extractive Sectors: Challenges and Considerations for African Countries	Kinda Mohamadieh and Daniel Uribe
66	March 2016	The Bolar Exception: Legislative Models And Drafting Options	Carlos M. Correa
67	June 2016	Innovation and Global Intellectual Property Regulatory Regimes – The Tension between Protection and Access in Africa	Nirmalya Syam and Viviana Muñoz Tellez
68	June 2016	Approaches to International Investment Protection: Divergent Approaches between the TPPA and Developing Countries' Model Investment Treaties	Kinda Mohamadieh and Daniel Uribe
69	July 2016	Intellectual Property and Access to Science	Carlos M. Correa
70	August 2016	Innovation and the Global Expansion of Intellectual Property Rights: Unfulfilled Promises	Carlos M. Correa
71	October 2016	Recovering Sovereignty Over Natural Resources: The Cases of Bolivia and Ecuador	Humberto Campodonico
72	November 2016	Is the Right to use Trademarks Mandated by the TRIPS Agreement?	Carlos M. Correa

73	February 2017	Inequality, Financialization and Stagnation	Yılmaz Akyüz
74	February 2017	Mitigating The Regulatory Constraints Imposed By Intellectual Property Rules Under Free Trade Agreements	Carlos M. Correa
75	March 2017	Implementing Farmers' Rights Relating to Seeds	Carlos M. Correa
76	May 2017	The Financial Crisis and the Global South: Impact and Prospects	Yılmaz Akyüz and Vicente Paolo B. Yu III



**SOUTH
CENTRE**

**Chemin du Champ d'Anier 17
PO Box 228, 1211 Geneva 19
Switzerland**

**Telephone: (41 22) 791 8050
Fax: (41 22) 798 8531
Email: south@southcentre.int**

**Website:
<http://www.southcentre.int>**

ISSN 1819-6926