Rethinking Global Pharmaceutical Policy

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Chapter 7: Voluntary Licensing[1]

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The previous chapter explored ways in which increased usage of the power of pharmaceutical firms to differentiate among consumers in the prices they charge for their own products could help address the global health crisis. This chapter explores an alternative way in which the firms might contribute to the increased availability of affordable drugs in poor countries: licensing other manufacturers to use their proprietary technology to produce generic versions of their products and then sell them at low prices in low and middle-income countries.

Section A describes the history of this approach. Section B distills from that narrative a set of guidelines that could increase both usage of the approach and its benefits for global health.

A. History

The technique of what has come to be known as "voluntary licensing" was developed and refined in three overlapping phases. In the first, it was used to increase the availability of treatments for HIV. In the second, it was used by some of the firms that developed direct-acting antiviral drugs aimed at Hepatitis C. Finally, it was employed to augment the availability in poor countries of therapeutic drugs for COVID-19. The three tales are told below. (Each narrative contains more details than are essential to understand the roles placed by voluntary licensing in the pharmaceutical ecosystem; they are included because they will provide grist for mills we bring forward in subsequent chapters.)

1. ARVs

Chapter 2 discussed how, beginning in 1987, a series of increasingly effective anti-retroviral drugs (and combinations thereof) designed to mitigate HIV were developed by pharmaceutical firms and approved by regulatory agencies, making it possible for infected persons to survive and to live normal lives. From the beginning of the AIDS pandemic, the large majority of infected persons were located in low-income and lower-middle-income countries, most of them in sub-Saharan Africa. However, the prices at which the ARVs were first introduced (typically between US$10,000 and US$15,000 per year for an adult patient) made them unaffordable for patients in those countries or for the countries'

[1] This chapter is an updated and revised version of a 2023 report by the John C. Martin Task Force, entitled "Voluntary Licensing and Access to Medicines." The original report, available at https://ipxcourses.org/GAiA/VLAM_Report_v1.1.pdf, was co-authored with Claudio Lilienfeld, Ruth Okediji, Clifford Samuel, Kenneth Shotts, and Abraham D. Sofaer. The portions of the report that have survived the revision are reprinted here with the co-authors' permission. However, they should not be blamed for the changes.

public-health services. As a result, the death rates from AIDS in those countries continued to rise rapidly even after ARVs became available, provoking intensified demands that the companies holding the IP rights to the drugs lower their prices.

A series of events in the 1990s reinforced those demands: Several pharmaceutical firms attempted to prevent South Africa from imposing a compulsory license on their patents, which produced a public-relations backlash;[2] generic drug manufacturers in India (where patents on pharmaceutical products were not available until recently) began producing ARV cocktails and selling them cheaply in other countries;[3] and the government of Brazil used its bargaining power to extract major price concessions from some of the pharmaceutical firms, which in turn enabled it to curb the HIV pandemic in that country.[4]

Into this fray entered the fledgling company, Gilead Sciences. Between its founding in 1987 and 2000, Gilead had developed drugs in a wide variety of sectors. After the turn of the century, it concentrated on antiviral drugs. Tenofovir, Gilead's pioneering HIV treatment, received FDA approval in 2001. Other ARVs soon followed. When the effectiveness of these drugs became apparent, AIDS activists began to demand that Gilead devise a way of making them available in poor countries. The CEO, John C. Martin, instructed Clifford Samuel, the leader of the relevant division in the company, to find a way to do so.

A crucial complement to the company's efforts was the availability of a massive amount of public funding to curb the pandemic. The principal sources of the money were the Global Fund to Fight AIDS, TB, and Malaria (launched in 2002) and the U.S. President's Emergency Program for AIDS Relief (PEPFAR) (launched in 2003). The sums that those programs, in combination, made available are shown in Figure 1, below. These funds not only procured medicines but augmented capacity (infrastructure and medical expertise) in the most affected countries.

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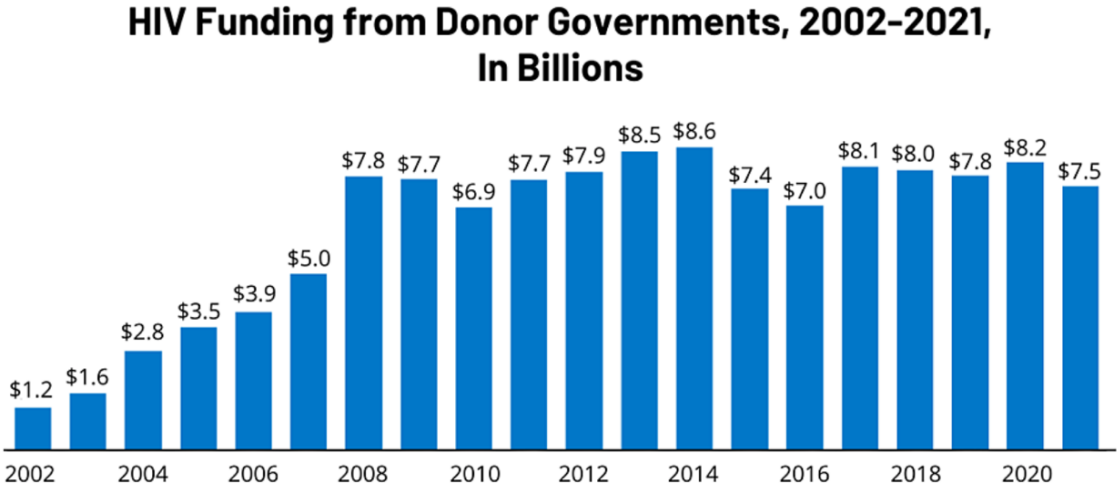
[2] See William Fisher and Cyrill P. Rigamonti, "The South Africa Aids Controversy: A Case Study in Patent Law and Policy," *Harvard Law School Case Study* (2005), https://ipxcourses.org/GPP/South_Africa_AIDS_Controversy.pdf.

[3] See AVERT, "Antiretroviral Drug Prices," http://www.avert.org/antiretroviral-drug-prices.htm.

[4] See Adele S. Benzaken, Gerson F.M. Pereira, and Lendel Costa, "Antiretroviral Treatment, Government Policy and Economy of Hiv/Aids in Brazil: Is It Time for Hiv Cure in the Country?," *AIDS Research and Therapy* 16, no. 19 (2019).

Figure 1[5]



Despite the magnitude of these funds, it quickly became apparent that, if Gilead wished to reach the rapidly growing population of infected persons in LMICs, it would have to lower the prices of its products in those countries. Starting in 2003, the company tried to do so by distributing its own branded products in those markets at no-profit prices.[6] Other companies that had developed ARVs, such as Merck and GlaxoSmithKline, adopted similar "tiered" pricing policies for their branded products at the same time. The results were disappointing; too few buyers could afford the branded products manufactured by Gilead – even at no-profit prices. Activists' criticism of Gilead's efforts intensified.[7]

In 2006, Gilead shifted to a strategy based upon licensing. This strategy was not altogether novel. A few companies had previously issued so-called "non-assertion" declarations (pledges not to enforce their intellectual property rights in specified jurisdictions) or licenses to generic manufacturers for below-market royalty rates. But these were typically limited in their coverage or "quasi-commercial" in character.[8] Gilead went further. Under Samuel's leadership, the company began to issue licenses whose primary objective was maximization of access to its products in poor countries.

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[5] Source: KFF and UNAIDS, "Donor Governments Spent US$7.5 Billion on Efforts to Combat HIV/AIDS Globally in 2021, Largely Flat Amid the COVID-19 Pandemic, KFF-UNAID Report Finds" (July 22, 2022), https://www.kff.org/global-health-policy/press-release/donor-governments-spent-us7-5-billion-on-efforts-to-combat-hiv-aids-globally-in-2021-largely-flat-amid-the-covid-19-pandemic-kff-unaid-report-finds/

[6] More specifically, Gilead selected 11 distributors, which it then authorized to sell its branded ARVs in 130 low-income and emerging economies. Gilead charged the distributors no-profit prices, but allowed them to earn profits of 10 to 15% to cover the costs of registering the products in those countries and cultivating the local medical networks.

[7] See, e.g., Nicole Neroulias, "Activists: Deny Patent to Gilead," *East Bay Times*, May 11, 2006 2006.

[8] See Brook K. Baker, "A Sliver of Hope: Analyzing Voluntary Licenses to Accelerate Affordable Access to Medicines," *Northeastern University Law Review* 10, no. 2 (2018): 241-42.

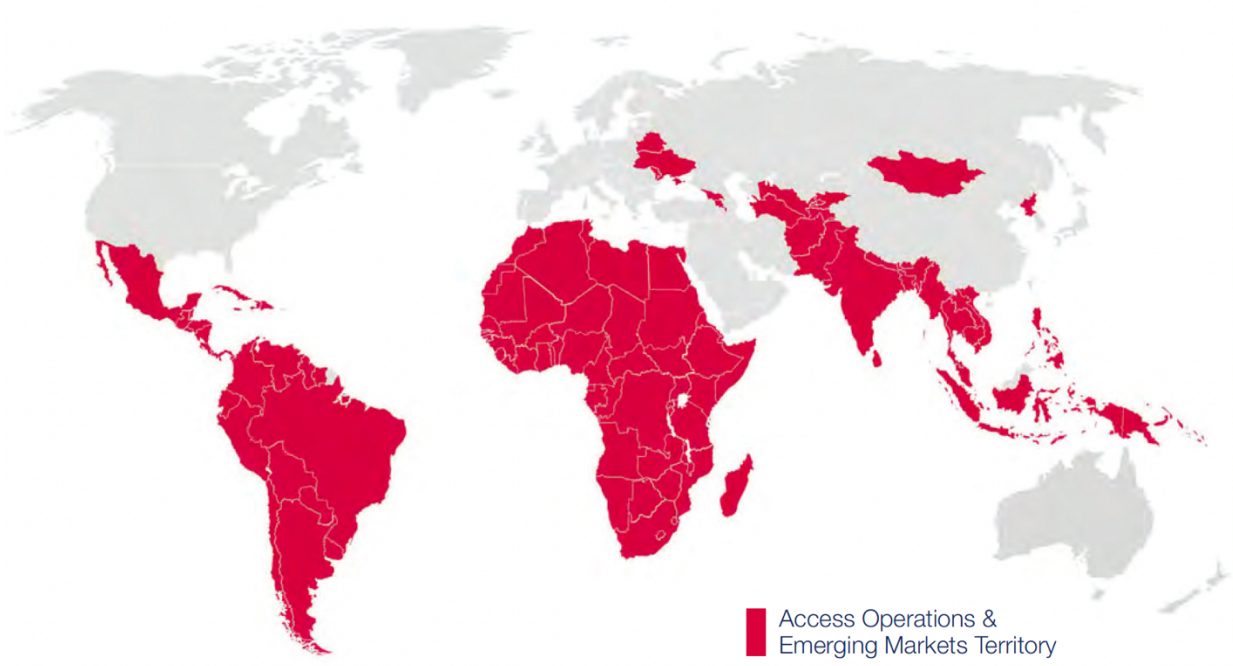
It took some time for Gilead to hone this approach. Early versions of the licenses contained some terms that activists regarded as anti-competitive,[9] and the geographic scope of the policy was initially modest. But the company eventually settled on the following model:

- A limited set of trusted generic manufacturers were authorized to produce tenofovir, all tenofovir combinations, and all future pipeline HIV products and to sell those products in – or export them to – specified countries;
- Low royalties – typically 5% of the licensees' sales on their finished products;
- Royalties waived on pediatric formulations;
- Broad fields of use (achieved by defining the set of "low-income" countries generously);
- Provisions forbidding diversions of products to other jurisdictions;
- Licensees are free to set their own prices and to sell active pharmaceutical ingredients (APIs) (royalty-free) to each other;
- Technology-transfer obligations – i.e., duties on the part of Gilead to transfer to the licensees the know-how necessary to manufacture the products;
- Quality standards: Licensees agree to seek WHO Prequalification, EMA or Tentative FDA approval;
- Close coordination with LMIC governments and NGOs;[10]
- Implementation of an "awareness and advocacy" campaign in targeted LMICs; and
- Transparency (the terms of all of the licenses were made public).

[9] See ibid., 247-48; Knowledge Ecology International, "Kei Asks Ftc to Investigate Gilead Effort to Control Market for Aids Drugs Ingredients," news release, February 15, 2007, https://perma.cc/N4Q3-X3SA.

[10] Programs implemented by Gilead included studies of disease burden across the various geographies, support for medical education and training, and help to secure diagnostic capabilities.

Figure 2, below, shows the countries covered by this policy in its final form.



In 2010, the emergence of the Medicines Patent Pool (MPP) enabled Gilead to modify and extent this policy. Created by UNITAID, the MPP was intended to be a global "public health organization with a mandate to accelerate access to affordable and quality-assured treatments in developing countries through an innovative voluntary licensing . . . and patent pooling mechanism."[11] The MPP soon began negotiating licenses with innovators and then issuing sub-licenses to generic licensees, facilitating the entry of pharmaceutical products into countries where innovators lack presence.

The MPP's practices also matured gradually. The model upon which it eventually settled included many systems designed to supplement the negotiated licenses. For example, it employs tracking mechanisms to prevent generic versions of the originator's drugs from being diverted to developed-country markets through an "Alliance Management System" (AMS). AMS supports the sub-licensees in their development and registration activities and monitors them to ensure that they abide by the terms of the head license – i.e., the license that the MPP had negotiated with the originator. In addition, the MPP works with governments and other stakeholders to ensure the licenses result in product access on the ground.[12]

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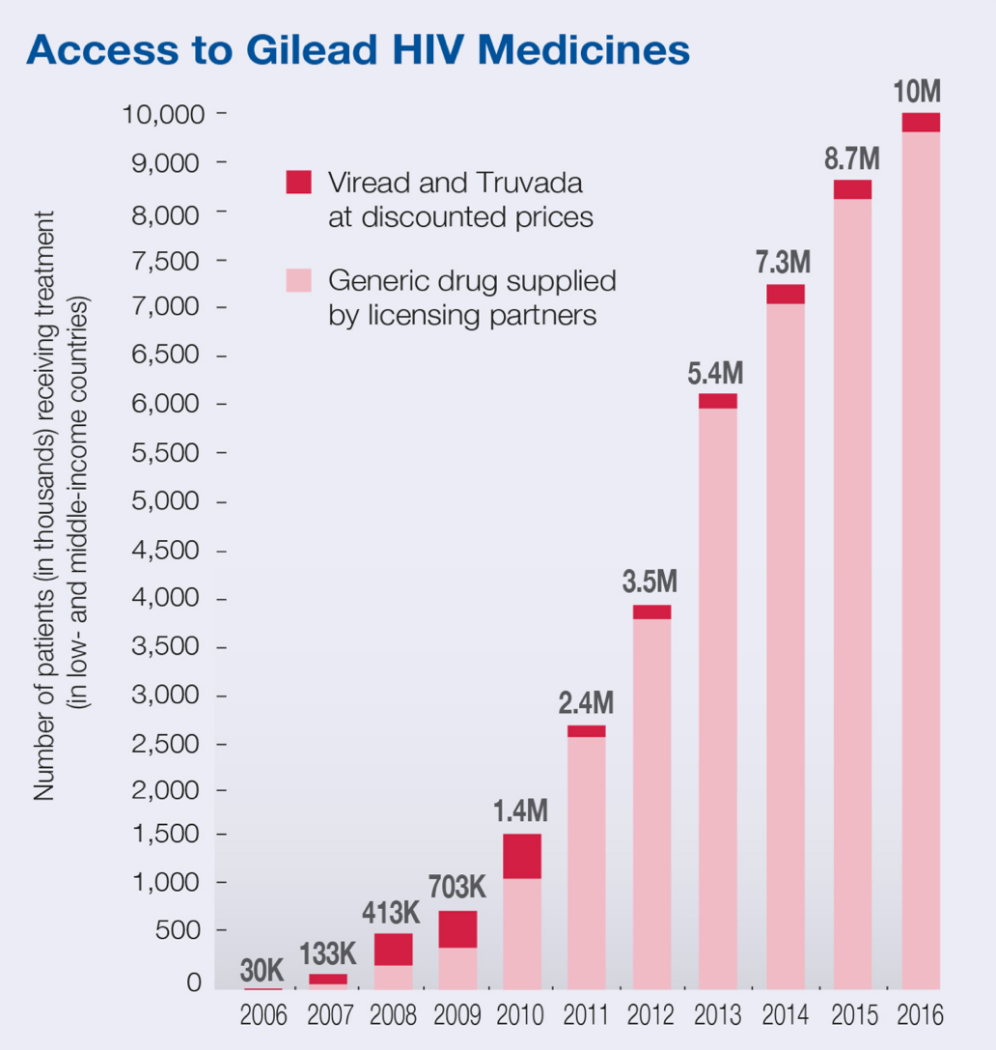
[11] Medicines Patent Pool, "Report to the Who Expert Committee on the Selection and Use of Essential Medicines," (2019).

[12] See William Looney, "The Medicines Patent Pool Plots a Post-Pandemic Future: Interview with Director Charles Gore," *In Vivo*, September 20, 2021; Charles Gore et al., "Negotiating Public-Health Intellectual

Gilead soon took advantage of this combination of services and began issuing licenses through the MPP as well as continuing to negotiate bilateral licenses directly. This composite approach proved highly successful. The prices of Gilead's HIV drugs in LMICs dropped from $20/month to $4/month. The number of people treated globally with Gilead's HIV medicines increased from tens of thousands in the mid-2000s to more than 20 million in 2023. As Figure 3 shows, over time a growing percentage of those drugs consisted of generic products produced pursuant to voluntary licenses, rather than Gilead-manufactured branded products.

Property Licensing Agreements to Increase Access to Health Technologies: An Insider's Story," *BMJ global health* 8, no. 9 (2023).

Figure 3[13]



Two factors seem to have been especially important in the success of the voluntary-licensing strategy. First, the generic companies to which the licenses were issued proved capable of manufacturing the ARVs more cheaply than could Gilead. Second, the Global Fund and PEPFAR radically increased procurement of first-line ARVs in the effort to pursue their "90/90/90 Treatment for All" campaign.[14]

Although the adoption of Gilead's strategy was substantially motivated by altruism, it was – and remains – commercially viable. For example, between 2014 and 2018, Gilead earned, from its "Access and Emerging Markets" program, gross revenues of $2.2 billion

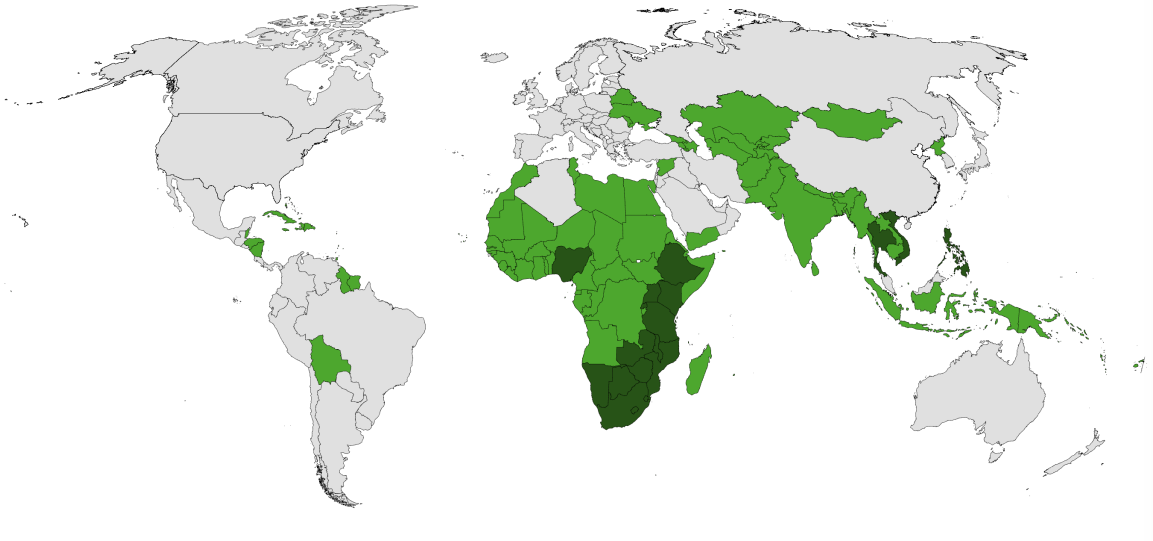
[13] Source: https://www.gilead.com/-/media/files/pdfs/other/hiv%20access%20backgrounder%20us%20112816.pdf. See also Gilead Sciences, "Impact Report: Access Operations and Emerging Markets," (2017).

[14] See Jacob Levi et al., "Can the Unaids 90-90-90 Target Be Achieved? A Systematic Analysis of National Hiv Treatment Cascades," *BMJ global health* 1, no. 2 (2016).

from sales of its branded products and $29 million in the form of royalties from generic licensees.

The most recent of Gilead's HIV voluntary licenses pertains to lenacapavir, the injectable drug discussed in Chapter 2 that has proven to be so effective both in treating persons with drug-resistant infections and in preventing infections altogether. Lenacapavir is currently on sale in the United States for $42,250 per one-year course of treatment. Aware that such a price would make it altogether unaffordable in the regions where HIV is most prevalent, Gilead recently licensed six manufacturers to produce generic versions of lenacapavir and distribute them in a "Territory" that includes 120 countries.[15] Three of the licensees are based in India, one each in Pakistan, Egypt, and the United States. The countries in which distribution of the generics is authorized are shown in the following map.

Figure 4: Countries included in the Voluntary License for Lenacapavir



The lenapacivir license contains a novel provision. Within the overall Territory, it identifies 18 countries (shown in dark green) where HIV prevalence is especially high and resources are especially low. The license then provides that, if any of the licensees is able within three years to obtain marketing approval for its generic products in all 18 countries, Gilead "will consider appointing Licensee as a preferred partner … with respect to any future product formulation of Lenacapavir which Gilead is intending to license."[16] This

[15] See Owen Dyer, "Gilead to License Generic Lenacapavir for Hiv Prophylaxis in 120 Lower Income Countries," *BMJ (Online)* 387 (2024); Gilead, "Gilead Signs Royalty-Free Voluntary Licensing Agreements with Six Generic Manufacturers to Increase Access to Lenacapavir for Hiv Prevention in High-Incidence, Resource-Limited Countries," news release, 2024, https://perma.cc/4U9L-NSAW. The license itself is available at https://perma.cc/4FXN-CRFR.

[16] Section 7.3(a).

promise is vague, but its purpose is clear enough: to encourage the licensees to extend their reach into the most needy countries.

Unfortunately, the set of countries covered by the lenacapaivir license is significantly smaller than the set (shown in Figure 3, above) covered by the HIV licenses issued previously by Gilead. Notably absent are some middle-income countries in Latin America and Eastern Europe where, as Chapter 1 discussed, HIV is now spreading especially fast. Indeed, in some of those countries – Argentina, Brazil, Mexico and Peru – Gilead had conducted clinical trials on lenacapavir and yet has not given their residents the benefit of the new license.[17] These exclusions have exposed the company to sharp criticism. But within the Territory, the license will undoubtedly be highly beneficial.

Gilead has surely not been the only actor in the campaign against AIDS. As indicated above, the success of that campaign has depended heavily on the massive infusion of funds from donor countries. In addition, other pharmaceutical firms have initiated similar access-oriented policies. Some, like Gilead, negotiated licenses directly with generic manufacturers, but a growing percentage have relied instead on the brokerage services of the MPP.[18] Finally, as the patents on the early ARVs expired, some firms have produced and sold generic versions of them without licenses.

The net result has been a remarkable decline in the prices of AIDS drugs in poor countries and an associated expansion of the set of people able to obtain treatment. In 2023, Charles Gore, the director of the MPP, was able to report that:

> [T]he price of WHO-recommended daily first-line fixed-dose combination HIV treatment (tenofovir/lamivudine/dolutegravir) is now less than US$50 per person per year: less than US$1 per week.[19]

2. Hepatitis C

Hepatitis C (HCV) is a viral liver infection typically spread through contact with infected blood, most often as a result of drug use or unsafe sexual practices. A minority of the people who are infected by the virus recover fully without treatment. In the majority of cases, however, the infection becomes chronic. Symptoms typically appear many years after an initial acute phase, after the liver has been damaged. They include fatigue,

[17] See Rick Guasco, "Gilead Licenses Generic Version of Lenacapavir as Prep in 120 Countries Outside the U.S.," *Positively Aware* (2024), https://perma.cc/EH72-EY99.

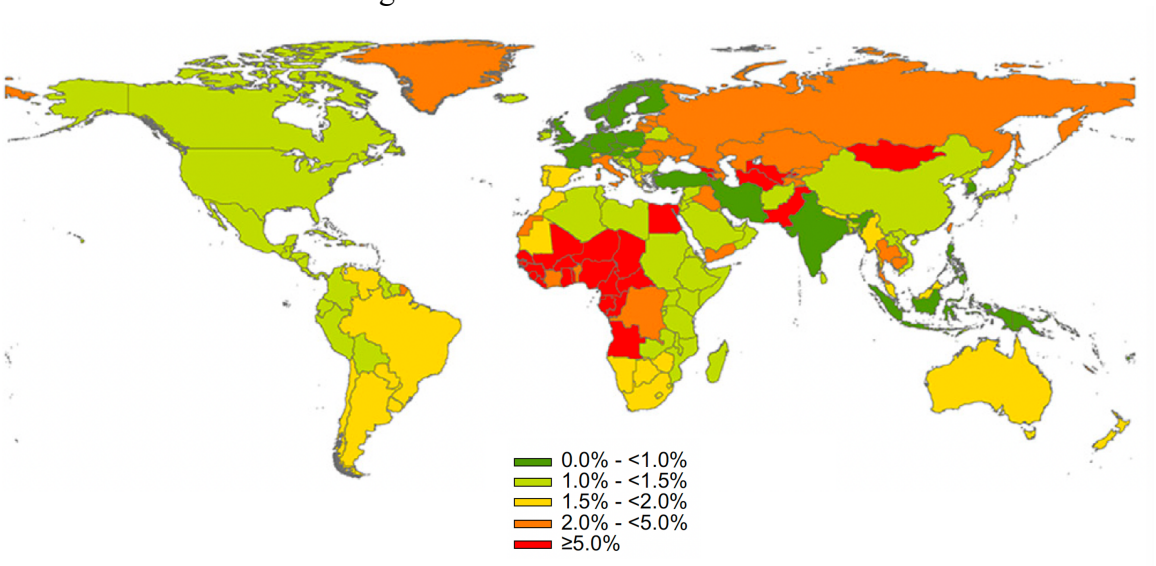
[18] See Gore et al., "Negotiating License Agreements," 1; MPP, "Voluntary Licensing: Right for Health, Smart for Business," (2024); Looney, "Medicines Patent Pool."

[19] Gore et al., "Negotiating License Agreements," 1.

jaundice, weight loss, and drowsiness. In a subset of those cases, the disease progresses to cirrhosis or liver cancer, which are often fatal.[20]

Estimates of the global prevalence rate of HCV vary considerably, because so many infections go undetected. As of 2013 (an important date, for reasons that will soon become clear), approximately 1.6% of the global adult population were infected – in the specific sense that they carried antibodies for the HCV virus. Translated into numbers, that means that roughly 115 million people were infected.[21] The distribution among countries is shown below:

Figure 5: HCV Adult Prevalence[22]



Until 2011, the standard treatment for HCV was a combination of pegylated interferon and ribavirin. Those drugs did not attack the virus directly, but rather worked by stimulating the body's own immune system.[23] This approach had several disadvantages: it was inconvenient (because the interferon had to be administered through weekly injections); it had serious side effects (flu-like symptoms, anemia, neutropenia, rash, and

[20] See WHO, "Hepatitis C," https://perma.cc/4AQZ-54JP; "Accelerating Access to Hepatitis C Diagnostics and Treatment: Overcoming Barriers in Low and Middle-Income Countries," (2020).

[21] See Erin Gower et al., "Global Epidemiology and Genotype Distribution of the Hepatitis C Virus Infection," *Journal of hepatology* 61, no. 1 (2014). For a substantially higher estimate of the global prevalence rate, see Arnolfo Petruzziello et al., "Global Epidemiology of Hepatitis C Virus Infection: An up-Date of the Distribution and Circulation of Hepatitis C Virus Genotypes," *World Journal of Gastroenterology* 22, no. 34 (2016). The WHO's estimate of the number of people with chronic infections was also a bit higher than Gower's: between 135 and 150 million. See Mohga Kamal-Yanni, "Hepatitis C Drug Affordability," *The Lancet global health* 3, no. 2 (2015).

[22] Source: Gower et al., "Global Epidemiology and Genotype Distribution of the Hepatitis C Virus Infection," S52. To estimate the prevalence rates in countries lacking good data, Gower et al. extrapolated from other countries in the region.

[23] See Libin Rong and Alan S. Perelson, "Treatment of Hepatitis C Virus Infection with Interferon and Small Molecule Direct Antivirals: Viral Kinetics and Modeling," *Critical reviews in immunology* 30, no. 2 (2010).

depression); and it was only moderately effective.[24] In 2011, clinical trials of two molecules that, unlike the standard treatment, directly addressed the HCV virus showed considerable promise. However, they too had disadvantages; they had to be taken with interferon and ribavirin; they had significant side effects; and they were only effective against one of the genotypes of the virus.[25]

2013 witnessed a breakthrough. Once again, the key institutional actor was Gilead. Two years previously, Gilead had purchased (for $11 billion) from Pharmasset (a small biotech firm) the rights to sofosbuvir, another direct-acting anti-viral ("DAA").[26] Clinical trials demonstrated the capacity of sofosbuvir, not just to suppress the disease, but to cure patients altogether in over 90% of the cases. Side effects were minimal, and, because it could be administered orally (once a day), treatment was convenient and inexpensive. In December of 2013, the FDA approved the drug. Gilead began selling it in the United States (under the brand name, Sovaldi) for a startling price -- $84,000 for a 12-week course of treatment. Shortly thereafter, the EMA approved it, and Gilead began negotiating prices with European governments. Among the outcomes of those negotiations: 50,426 Euros for a course of treatment in Germany, 41,680 Euros in France, and 13,000 Euros in Spain.[27]

The prices charged by Gilead in the United States and Europe proved highly controversial. The company defended them on the ground that, by curing the disease, sofosbuvir enabled recipients not only to avoid years of misery, but also to save the costs of late-stage treatments, such as liver transplants. Not everyone was convinced. In the United States, Congress convened hearings to consider the legitimacy of Gilead's fees.[28] In Europe, Gilead's approach was sharply criticized by both governments and activist organizations. In both markets, however, most of the resistance eventually subsided, and Gilead maintained course.

In the ensuing decade, other similar or complementary HCV drugs became available. Gilead itself developed some of them. For example, a combination of sofosbuvir and ledipasvir proved even better than sofosbuvir alone, so Gilead began selling the combination (under the brand name, Harvoni) – for an even higher price. Bristol Myers

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[24] See V. Kasturi Rangam, "Gilead: Hepatitis C Access Strategy (a)," (Harvard Business School Case Study 9-515-025, 2023), 5.

[25] The molecules in question were boceprevir (developed by Merck) and telaprevir (developed by Vertex). See ibid., 6. For discussion of their limitations, see Imam Waked, "Case Study of Hepatitis C Virus Control in Egypt: Impact of Access Program," *Antiviral therapy* 27, no. 2 (2022): 2.

[26] For the history of Pharmasset – and the role of public funding in supporting the research of its founder, see Hep C Coalition, "Sofosbuvir Turns 5 Years Old: The Vast Majority of People with Chronic Hepatitis C Still Have Not Been Treated," (2018), 7.

[27] See MSF, "Not Even Close," (2017): 3; Germán Velásquez, "The Use of Trips Flexibilities for the Access to Hepatitis C Treatment," (South Centre, 2018), 4.

[28] See, e.g., Margot Sanger-Katz, "$1,000 Hepatitis Pill Shows Why Fixing Health Costs Is So Hard," *New York Times*, August 2, 2014 2014.

Squib (BMS) entered the field with a different compound, daclatasvir ("DCV"), which, when matched with sofosbuvir, also improved its operation.[29]

Starting in 2013, when the potential benefits of the DAAs became apparent, Gilead and (later) BMS began formulating a strategy that would enable them both to sustain their high prices in their principal markets and to make their products available at lower prices outside of wealthy countries, where the large majority of the people infected with HCV resided. In its mature form, that strategy had two major components, each with several subparts.

The first component was a set of legal shields designed to limit competition and thus to protect the companies' power to set prices for the pioneering drugs. Three forms of protection were most important. The first was a robust set of patents – product patents on the drugs themselves and supplementary patents on improvements, dosages, etc. Gilead and BMS applied for such patents in most high-income and middle-income countries, and most of those applications were granted. In a few countries, however, they were rejected, on the ground that they failed the novelty or inventive-step requirements.[30] Second, relying on the tactic discussed in Chapter 2, the companies either delayed or forewent altogether applying for regulatory approval in many countries. Absent such approval, the drugs of course could not be distributed there.[31] Finally, in countries in which the companies did seek and obtain regulatory approval, they relied on data-exclusivity protection to impede the subsequent introduction of generic substitutes, even if patents had not been granted in those jurisdictions.[32]

The second component of the companies' strategy was a pair of business practices designed to increase the affordability and thus the availability of the drugs in poor countries. The first of those practices was geographic differential pricing – one of the techniques discussed in detail in the previous chapter. In 2013, Gilead announced three "tiers" of prices for Sovaldi – the lowest price offered to the poorest countries (most of them located in subSaharan Africa), a higher price for lower-middle-income countries (including Egypt, which we will discuss shortly), and so forth. The second practice – and the one most relevant to the topic of this chapter – was a system of voluntary licenses closely analogous to the system that Gilead had developed for HIV drugs. In September of 2014, the company granted licenses to seven manufacturers based in India, authorizing them to distribute in 91 countries generic versions of both sofosbuvir and a single-tablet

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[29] See MSF, "Not Even Close," 3.

[30] The status as of 2016 of the patent portfolios on all of the new DAA drugs are described in the following set of reports: WHO, "Patent Situation of Key Products for Treatment of Hepatitis C: Sofosbuvir," (2016); "Patent Situation of Key Products for Treatment of Hepatitis C: Simeprevir," (2016); "Patent Situation of Key Products for Treatment of Hepatitis C: Daclatasvir," (2016); "Patent Situation of Key Products for Treatment of Hepatitis C: Ledipasvir," (2016); "Patent Situation of Key Products for Treatment of Hepatitis C: Paritaprevir/Ombitasvir/Dasabuvir," (2016). All are available through https://www.who.int/news/item/19-07-2016-who-updates-patent-information-on-treatments-for-hepatitis-c.

[31] See MSF, "Not Even Close," 7.

[32] See ibid., 5.

regimen of sofosbuvir combined with ledipasvir.[33] The royalty rate of this first wave of licenses was 7%. Gilead pledged to use the proceeds to cover costs associated with regulatory approvals and educational initiatives.[34] The licenses included both technology-transfer provisions (thus accelerating the availability of the generics in the covered territory) and anti-diversion provisions (intended to keep the inexpensive generics confined to that territory). The scope of the license was subsequently expanded to 14 licensees (located in India, Egypt, and Pakistan) and 101 countries, and then to 105 countries.[35] When other variants of sofosbuvir came online, Gilead extended the voluntary-licensing plan to cover them. BMS adopted a similar approach, but granted its licenses through the MPP, rather than directly. Abbvie did the same for its (less popular) entry into the field, a combination of glecaprevir and pibrentasvir.[36]

These two components were intertwined in many ways. For example, a side-effect of the voluntary-licensing system was to reduce the competition that Gilead faced in jurisdictions not covered by the licenses. The reason: one of the terms of the contracts signed by the major Indian generic manufacturers was a pledge not to sell drugs in countries not included in the license. Voluntary licensing also functioned in part as a means of defusing the criticism that the companies received for the prices they charged in markets outside the VL footprint. On one occasion, the VL system also functioned as a safety valve; In response to especially sharp criticism of the prices that it was charging in Belarus, Malaysia, Thailand and Ukraine – and to threats by Malaysia to impose a compulsory license on its patent – Gilead agreed to expand the geographic scope of the voluntary license to reach those countries.[37]

So how well did this system work? From the companies' standpoint, very well indeed. Estimates of the profits that the companies made from sales of the new HCV drugs vary, but all are high. For example, one reported that, in the first five years following FDA approval of sofosbuvir, Gilead made a profit of $25 billion from its HCV drugs.[38]

In one especially important country, the public at large also benefitted enormously. That country was Egypt. The reason for its importance is that, as of 2013, Egypt had by

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[33] See Gilead Sciences, "Chronic Hepatitis C Treatment Expansion," news release, October 20, 2014, 2014, https://perma.cc/S9V2-DKC9.

[34] See V. Kasturi Rangan, "Gilead: Hepatitis C Access Strategy (B)," in *Harvard Business School Case Study 9-515-044* (2016).

[35] See Gilead Sciences, "Chronic Hepatitis C Treatment Expansion," news release, November 17, 2017, 2017, https://perma.cc/QEL6-NB7M.

[36] See MSF, "Not Even Close," 5; WHO, "Accelerating Access to Hepatitis C Treatment," 28.

[37] See Fifa Rahman, "Malaysia Inclusion in Gilead Voluntary Licence – a Product of Compulsory Licence Pressure," *Health Policy Watch* (2017), https://perma.cc/MGN7-938K. However, sales to those four countries were accompanied by a royalty rate of 12%, instead of the standard 7%. See Gilead Sciences, "2017 Amended & Restated Voluntary Hcv License Agreement," (2017), https://www.gilead.com/-/media/files/pdfs/other/form-ar-hcv-license-agmt-gild-11202017.pdf?la=en&hash=EA13A53F28CE66946255B7369B57EEFE.

[38] See Coalition, "Sofosbuvir Turns 5." For other estimates, see Velásquez, "Access to Hepatitis C Treatment," 4.

far the highest prevalence of HCV in the world. In the country at large, it was roughly 15%, and in some regions it was as high as 28%.[39] 40,000 of the country's residents died from the disease each year.[40] The reason for this extraordinary burden is that a 20th-century national vaccination program for schistosomiasis had been conducted poorly; inadequate sterilization of needles had allowed the virus to spread rapidly.[41]

In 2006, the government of Egypt convened a group of experts to study ways of limiting the impact of the HCV outbreak. Relying on the recommendations of that group, the Ministry of Health created a network of centers for treating infected persons with a combination of interferon and ribavirin.[42] As indicated above, that regimen was imperfect. It was especially unsatisfactory in Egypt, because the variant of HCV against which it is least effective is genotype 4, which happened to be the most common in that country.[43] This approach was also extraordinary expensive, consuming roughly 20% of the Ministry's annual budget.[44]

In 2013, when Sovaldi's potential power became apparent, the Ministry moved quickly to obtain supplies of the drug. Gilead initially offered it a price of $15,000 for a 12-week course of treatment. By emphasizing the severity of the epidemic in Egypt, representatives of the Ministry were able to persuade Gilead's executives to offer them instead the lowest-tier price: $900 for a 12-week supply (approximately 1% of the price in the United States).[45] To deploy the drugs as quickly as possible, the government waived the requirement for independent clinical trials and approved it for distribution a mere seven months after the FDA had approved it.[46] Gilead then collaborated with the Ministry on many levels – formulating testing and treatment plans, developing an educational program to alert both clinicians and potential patients concerning the new testing and treatment options, and of course delivering growing quantities of drugs.[47]

Soon thereafter, the fruits of the voluntary-licensing programs became apparent. Two Egyptian firms – Magic Pharma and Pharmed Healthcare – relying on licenses from

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[39] See Heba Wanis, "Egypt Will Not Patent New Hepatitis C Drug," (2014), https://perma.cc/BSK5-NVMN; Ahmed Hassanin et al., "Egypt's Ambitious Strategy to Eliminate Hepatitis C Virus: A Case Study," *Global health science and practice* 9, no. 1 (2021): 190.

[40] See Hazem Abosheaishaa et al., "The Egyptian Journey from Having the Highest Prevalence of Hepatitis C Virus to Being the First to Achieve "Gold Tier" in Conquering the Disease," *Proceedings - Baylor University. Medical Center* 37, no. 5 (2024).

[41] See Christina Frank et al., "The Role of Parenteral Antischistosomal Therapy in the Spread of Hepatitis C Virus in Egypt," *The Lancet* 355, no. 9207 (2000).

[42] See Waked, "Case Study of Hepatitis C in Egypt."; Hassanin et al., "Egypt's Strategy to Eliminate Hepatitis C," 191.

[43] See Rong and Perelson, "Treatment of Hepatitis C Virus Infection with Interferon and Small Molecule Direct Antivirals: Viral Kinetics and Modeling."

[44] See Rangan, "Gilead: Hepatitis C Access Strategy (B)."

[45] See Waked, "Case Study of Hepatitis C in Egypt," 2.

[46] Rangam, "Gilead: Hepatitis C Access Strategy (a)," 11.

[47] See Rangan, "Gilead: Hepatitis C Access Strategy (B)."

Gilead, began supplying the Ministry with generic versions, and the price of a 12-week course dropped sharply. By 2018, it had declined from $900 to $84 for the 12-week course.[48]

Between 2014 and 2020, the Ministry capitalized on the availability of the inexpensive drugs to construct and execute a comprehensive plan to purge the country of HCV. It set up myriad testing facilities, trained thousands of clinicians to do the testing and to administer drugs to persons who tested positive, and advertised the initiative heavily.[49] Most of the costs of the program were born by the Ministry. (In 2018, the Ministry received a loan of $530M from the World Bank, which covered a portion of the late stages of the project.)[50] By 2020, the program had tested more than 60 million people and provided treatment to over 4 million.[51] As a result, the prevalence rate of HCV in the country plummeted: to 4.61% in 2018, 2.39% in 2019; and 0.38% in 2023.[52] In 2023, Dr Tedros Adhanom Ghebreyesus, the Director-General of the World Health Organization, took note of the achievement:

> "Egypt's journey from having one of the world's highest rates of hepatitis C infection to being on the path to elimination in less than 10 years is nothing short of astounding. "Egypt is an example to the world of what can be achieved with modern tools, and political commitment at the highest level to use those tools to prevent infections and save lives. Egypt's success must give all of us hope and motivation to eliminate hepatitis C everywhere."[53]

Unfortunately, outside Egypt, far less progress has been made. Globally, the potentially game-changing availability of the DAA drugs starting in 2013 has had only a modest impact on the prevalence of chronic HCV or on the associated death rate. The discouraging numbers are shown below.

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[48] See Abosheaishaa et al., "The Egyptian Journey," 881; Waked, "Case Study of Hepatitis C in Egypt," 2.

[49] See "Case Study of Hepatitis C in Egypt," 3.

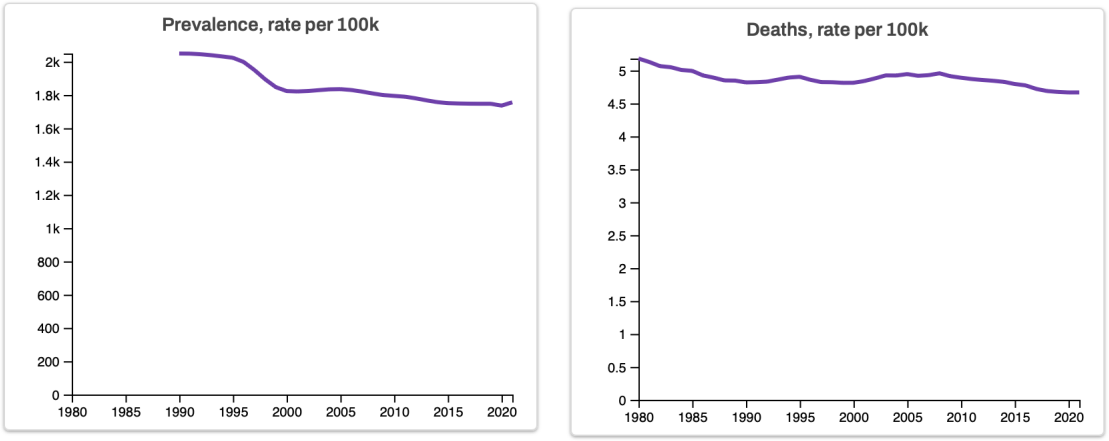
[50] See World Bank, "Transforming Egypt's Healthcare System Project," (2018).

[51] See World Economic Forum, "The Art and Science of Eliminating Hepatitis: Egypt's Experience," (2022), 5; Hassanin et al., "Egypt's Strategy to Eliminate Hepatitis C," 196.

[52] See Abosheaishaa et al., "The Egyptian Journey," 878. One of the physicians involved in the program from the beginning offers the following estimate of its costs and benefits: "Despite the large cost of the treatment program since 2014 and the cost of the screening and treatment program in 2018–2019, the economic return is huge. At a cost of US$ 350 million for treatment between 2014 and 2018, and US$ 207 million for the screening and treatment campaign in 2018–2019, the total economic gain in both direct and indirect costs is calculated to be more than US$ 7 billion between 2020 and 2030, or each US dollar spent in the program will result in an economic gain of more than US$ 11 over the following 10 years." Waked, "Case Study of Hepatitis C in Egypt," 5.

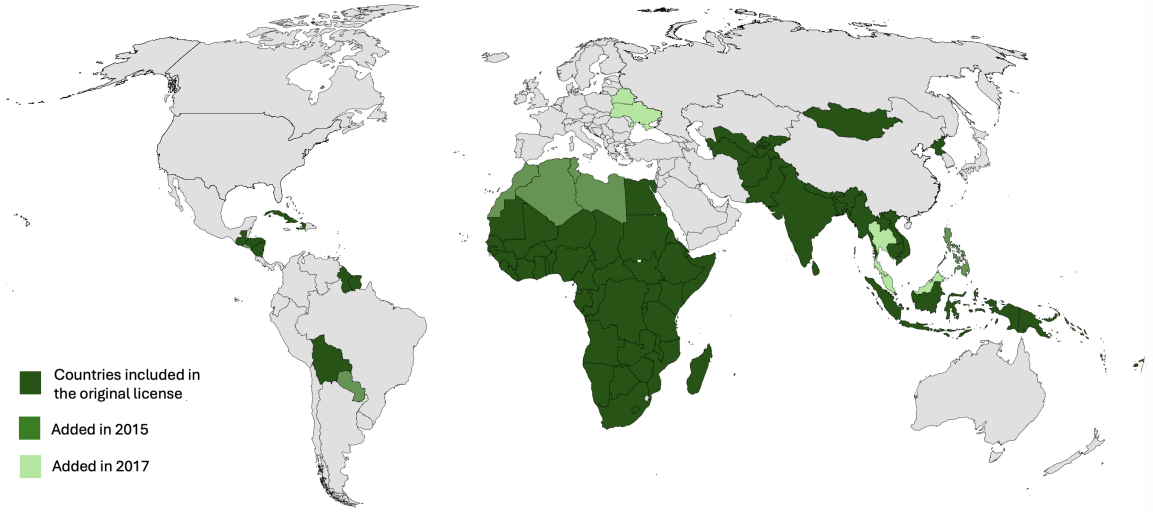
[53] WHO, "Egypt Becomes the First Country to Achieve Who Validation on the Path to Elimination of Hepatitis C," news release, October 9, 2023, 2023, https://perma.cc/KJZ9-J45S.

Figure 6: Global Prevalence of Chronic HCV and Associated Death Rate [54]



Several factors seem to underlie this disappointing outcome. The first is the limited scope of Gilead's voluntary-licensing system. Set forth below is a map of the coverage of the license – in other words, the countries in which the 14 licensees are permitted to sell generic versions of the drugs.

Figure 7: Countries included in the Voluntary License for Gilead's HCV Drugs



As one might expect, in most of these countries, generic HCV drugs are now available at modest prices.[55] The problem is that the majority of the people in the world infected with the virus do not reside in these countries and thus do not have access to the inexpensive drugs.

But what about the other part of the firms' access strategy? As indicated above, even before it instituted the voluntary-licensing system for HCV, Gilead adopted a

[54] Source: IMHE, https://vizhub.healthdata.org/gbd-results/.

[55] See, e.g., Isabelle Andrieux-Meyer et al., "Disparity in Market Prices for Hepatitis C Virus Direct-Acting Drugs," *The Lancet global health* 3, no. 11 (2015).

differential-pricing model, under which poorer countries were to be charged less for the branded versions of its drugs than were richer countries – and in each of the press releases since then Gilead has reiterated that commitment. Unfortunately, in practice, Gilead's adherence to the differential-pricing principle has proven to be haphazard at best. A 2020 study by Melissa Barber and colleagues compared the "originator prices" (i.e., the prices the companies charged for the branded versions) of the principal DAAs in the 50 countries where publicly accessible price databases could be found. As one might expect, those prices were much higher than those of the generics – and varied widely across countries.[56] Much more troubling was their finding that: "Across 50 countries, the pricing of originator DAAs has no apparent correlation to income level. Surprisingly, among high-income countries, pricing of all originator DAAs showed a moderately strong and statistically significant inverse correlation – countries with higher incomes have lower prices."[57] The most likely reason for that inverse correlation, the authors suggested, was simply that richer countries had stronger bargaining power.

In sum, in countries outside the footprint of the voluntary license, the high prices of the breakthrough DAAs make a comprehensive program of the sort deployed in Egypt impossible. Neither the public-health systems nor private insurers in those countries can afford to treat all infected people. So instead they typically ration the drugs – making them available only to people whose conditions have deteriorated substantially.[58] Infected persons can, of course, pay for the drugs out of pocket, but few have the necessary funds.[59] Transmissions from infected but relatively asymptomatic persons to naïve persons are thus allowed to continue. Despite these obstacles, in some countries growing percentages of

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[56] See Melissa J. Barber et al., "Price of a Hepatitis C Cure: Cost of Production and Current Prices for Direct-Acting Antivirals in 50 Countries," *Journal of Virus Eradication* 6, no. 3 (2020).: "The median originator price of sofosbuvir was US$40,502 per 12-week course, ranging from US$10,730 in Argentina to US$91,461 in Italy. The median price of daclatasvir across all countries was US$26,928 per 12-week course, ranging from US$3144 in Russia to US$100,415 in Italy. The median originator price of sofosbuvir/ledipasvir was US$46,812 per 12- week course, ranging from US$1249 in Morocco to US$73,771 in Latvia. The median price of sofosbuvir/velpatasvir was US$ 34,381 per 12-week course, ranging from US$10,368 in China to US$92,719 in Italy. The median price of lecaprevir/pibrentasvir was US$30,710 per 8-week course, ranging from US$15,628 in Brazil to US$89,485 in Canada."

[57] See ibid., 7. A similar lack of correlation between a country's wealth and the prices there of the DAAs is evident in the 2015 survey done by Andrieux-Meyer et al., "Disparity in Market Prices for Hepatitis C Virus Direct-Acting Drugs." and in the 2018 survey done by Swathi Iyengar et al., "Prices, Costs, and Affordability of New Medicines for Hepatitis C in 30 Countries: An Economic Analysis," *PLOS Medicine* 13, no. 5 (2016).(concluding that "Prices do not increase, and in some cases decrease, with increased standard of living.")

[58] See Alison D. Marshall et al., "Restrictions for Reimbursement of Interferon-Free Direct-Acting Antiviral Drugs for Hcv Infection in Europe," *THE LANCET GASTROENTEROLOGY AND HEPATOLOGY* 3, no. 2 (2018).

[59] See, e.g., Iyengar et al., "Prices of New Medicines for Hepatitis C," 12. ("The PPP-adjusted price of a full course of sofosbuvir alone would be equivalent to at least 1 year of the PPP-adjusted average earnings for individuals in 12 of the 30 countries analysed. In Poland, Slovakia, Portugal, and Turkey, a course of sofosbuvir alone would cost at least 2 years of average annual wages.")

infected people are receiving treatment. But the pace is far slower than in Egypt, in large part because of the costs of the drugs.[60]

In most of the countries inside the voluntary-licensing footprint, generic versions of the DAAs are cheap, just as they are in Egypt. There, the cause of the limited impact of the voluntary-licensing initiative seems to be a lack of foresight and political will. Gilead's representatives attempted to persuade representatives of some of the governments of the wisdom of Egypt's approach, but to no avail. In Pakistan, for instance, their entreaties fell on deaf ears. This lassitude, in turn, can be attributed in part to the absence of an organized and well-funded global eradication initiative comparable the one focused on HIV/AIDS.

The bottom line: despite the existence of a safe, risk-free course of treatment that is inexpensive to manufacture, the number of people suffering from chronic HCV who are cured each year in the world is less than the number of new infections. Roughly 250,000 people continue to die from the disease each year – needlessly.[61]

Three lessons can be derived from this phase of the strategy. First, the Egyptian story shows how a voluntary-licensing system can make drugs available at very low prices and in turn facilitate a campaign that eradicates a serious disease. Second, the lack of progress in other countries that lie within the GL footprint makes clear that low drug prices, though necessary for such a campaign, are not sufficient. Third, the high prices charged by Gilead and BMS outside of the VL footprint, seemingly without regard for ability of each country to pay, has enriched both companies, but at the cost of many lives.

[60] See WHO, "Accelerating Access to Hepatitis C Treatment," 7, 12-17; Karin Hepp Schwambach et al., "Cost and Effectiveness of the Treatment of Chronic Hepatitis C in Brazil: Real-World Data," *Value in health regional issues* 23 (2020); Ahmad Shakeri et al., "Spending on Hepatitis C Antivirals in the United States and Canada, 2014 to 2018," *Value in health* 23, no. 9 (2020).

[61] See WHO, "Hepatitis C". (estimating the number, in ___, at 242,000).

3. COVID

The technologies underlying the mRNA-based vaccines that proved so effective in combatting the COVID pandemic were developed over many years by scientists working in many institutions. Among the streams of research, the following were most important:[62]

- mRNA itself was first discovered in 1961. Speculation began soon thereafter concerning its potential for creating vaccines.
- In 1987, Robert Malone, working at the Salk Institute, found a way to induce human cells to translate mRNA and begin producing proteins.
- In 2000, Ingemar Hoerr, working at Tübingen University, was able to induce an immune response in mice by injecting them with mRNA. He later founded CureVac, a private firm focused on commercializing mRNA technology.
- In 2005, Katalin Karikó and Drew Weissman, working at the University of Pennsylvania, discovered that the substitution of pseudouridine for uridine could prevent an injection of synthetic mRNA from triggering an inflammatory immune response.
- In 2014, Pieter Cullis and colleagues, working at the University of British Columbia, developed a system for using lipid nanoparticles (LNPs) to stabilize mRNA, thereby enabling it to be delivered to target cells without degrading. Cullis then helped found two biotech companies in Canada: Arbutus Biopharma Corporation and Acuitas Therapeutics, Inc.

Several of the institutions in which these lines of research were conducted sought and obtained patents on their innovations.

Well before the COVID threat appeared, researchers at a few private firms – most notably, Moderna (based in Cambridge, Massachuetts), BioNTech (based in Mainz, Germany), and CureVac (based in Tübingen, Germany) – relying on these discoveries, began to develop vaccines aimed at various diseases. To do so, they typically obtained (either directly or through intermediaries) licenses to the patents obtained by their predecessors. As the firms refined the technologies, they sought patents of their own on their incremental innovations. By the end of the century, several of these non-COVID vaccine candidates were in early-stage clinical trials.[63]

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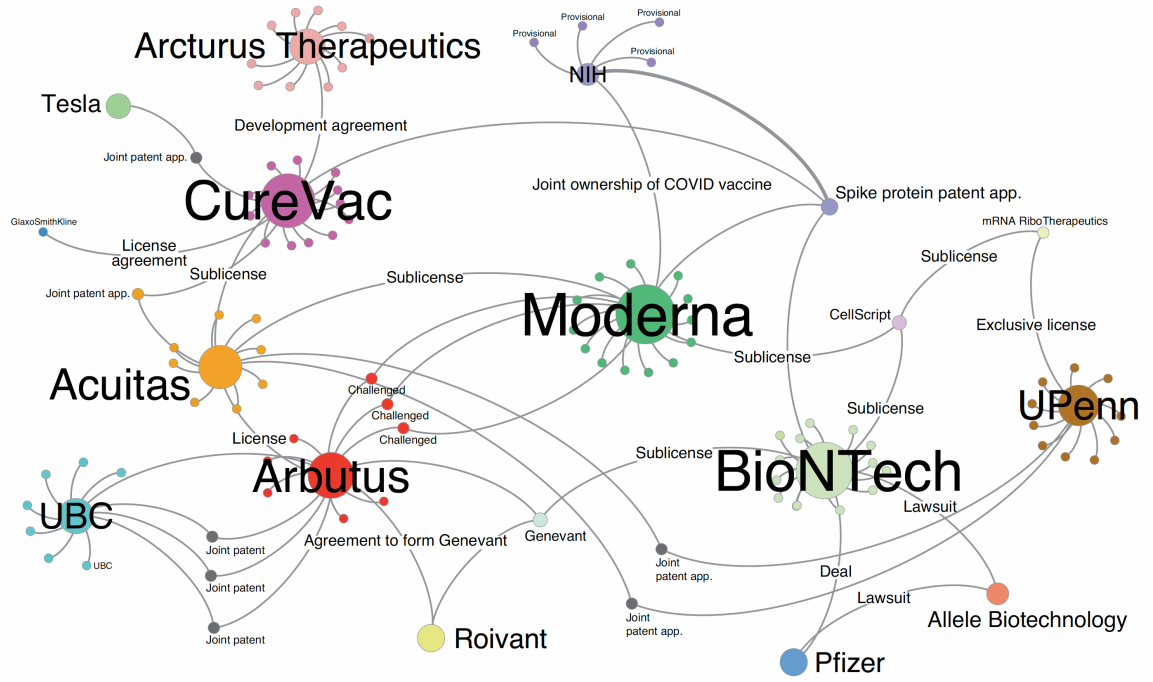
[62] The following chronology has been derived from: Robert Burrows and Ellen Lambrix, "Mrna Vaccines: A Growing and Complex Ip Landscape," *Vaccine Insights* 1, no. 4 (2022); Mario Gaviria and Burcu Kilic, "A Network Analysis of Covid-19 Mrna Vaccine Patents," *Nature biotechnology* 39, no. 5 (2021); Ulrich Storz, "The Covid-19 Vaccine Patent Race," ibid.40, no. 7 (2022).

[63] See Dan Shores, Dylan Haversack, and Andrew J. Storaska, "The Mrna Ip and Competitive Landscape through One Year of the Covid-19 Pandemic — Part I," *IP Watch* (2021), https://ipwatchdog.com/2021/04/11/mrna-ip-competitive-landscape-one-year-covid-19-pandemic-part/id=132130/; "The Mrna Ip and Competitive Landscape through One Year of the Covid-19 Pandemic — Part Ii," *IP Watch* (2021), https://ipwatchdog.com/2021/04/21/mrna-ip-competitive-landscape-translate-bio-arcturus-etherna-startups-lnp-technology-part-ii/id=132287/; "The Mrna Ip and Competitive Landscape

The emergence of the COVID virus prompted researchers at the three firms (as well as the National Institutes of Health) to accelerate their work, seeking to apply mRNA-based technology to develop vaccines to meet the new threat.[64] Almost immediately after the work began, all three firms sought patents on the potential fruits of their projects. Most of those initial applications were weak and are unlikely ultimately to pass muster. But as their work proceeded, the firms were able to obtain extensive portfolios of more durable patents. Some asserted rights to the APIs; others claimed supporting technologies, such as methods of use, optimal dosages, delivery systems, and manufacturing processes.[65]

The net result, by 2021, was an extraordinarily complex pattern of interlocking rights, well represented by the following diagram developed by Mario Gaviria and Burcu Kilic.

Figure 8[66]



through One Year of the Covid-19 Pandemic — Part Iii," *IP Watch* (2021), https://ipwatchdog.com/2021/04/30/mrna-patent-competitive-landscape-pioneers-litigation-outlook-big-pharmas-next-moves-part-iii/id=132936/; Burrows and Lambrix, "Mrna Vaccines."

[64] See Kizzmekia S. Corbett et al., "Sars-Cov-2 Mrna Vaccine Design Enabled by Prototype Pathogen Preparedness," *Nature (London)* 586, no. 7830 (2020); Storz, "The Covid-19 Vaccine Patent Race."

[65] See Shores, Haversack, and Storaska, "The Mrna Ip Landscape, Part 3"; Storz, "The Covid-19 Vaccine Patent Race."

[66] Source: Gaviria and Kilic, "A Network Analysis of Vaccine Patents." The authors' explanation of the diagram: "Large nodes represent the relevant entities while the edges represent agreements or patents between two entities. Smaller nodes around the entities represent patents that were identified as being relevant to the underlying vaccine technology." For a similar but less detailed diagram, see Shores, Haversack, and Storaska, "The Mrna Ip Landscape, Part 3". Figure 8.

Soon, tensions among these various players gave rise to opposition proceedings and infringement suits – both in the United States and in Europe. In some of these disputes, the defendants were accused of relying on patented technologies without permission; in others, the validity of the defendants' patents was challenged, either on the ground that they did not accurately identify all of the inventors of the technology in question or that they failed the novelty or inventive-step requirement. Many of those lawsuits are still ongoing, but they are unlikely to thin significantly the thicket of exclusive rights.[67]

The fights were counterbalanced, in part, by a growing set of collaboration agreements – the most important of which was a collaboration between BioNTech and Pfizer, which ultimately gave rise to the most commercially successful of the vaccines.[68]

Patents were not the only shields deployed by the firms. At least as important were trade secrets. The mRNA vaccines are substantially more complicated and difficult to produce than the HCV antivirals, discussed in the preceding section. Some of the supporting technologies, such as the LNP delivery systems, are also complex. To protect their competitive positions, the firms refused to reveal crucial details concerning this know-how.[69] Without access to it, other firms would have had great difficulty attempting to replicate the leaders' products.

Additional protections were provided by data-exclusivity rules, supply limitations, and the costs of securing regulatory approvals. In an interview, Stéphane Bancel, the CEO of Moderna, explained how these layers of protection interlocked:

> Drugmakers interested in manufacturing a similar mRNA vaccine would need to conduct the clinical trials, apply for authorization and then scale the manufacturing, which could take upward of 12 to 18 months, Bancel said. "This is a new technology," Bancel told analysts regarding mRNA. "You cannot go hire people who know how to make mRNA. Those people don't exist."[70]

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[67] For surveys of these suits, see Burrows and Lambrix, "Mrna Vaccines," 196-97; Storz, "The Covid-19 Vaccine Patent Race."; Gaviria and Kilic, "A Network Analysis of Vaccine Patents."; Shores, Haversack, and Storaska, "The Mrna Ip Landscape, Part 3".

[68] "Collaboration Agreement between Pfizer, Inc. And Biontech Se," (2020); Shores, Haversack, and Storaska, "The Mrna Ip Landscape, Part 3". For evidence of the commercial success of the BioNTech/Pfizer vaccine, see Global Commission for Post-Pandemic Policy, "Covid-19 Vaccine Production, to January 31st 2022," (2022).

[69] See Shores, Haversack, and Storaska, "The Mrna Ip Landscape, Part 3". (describing how Moderna improved upon the LNP delivery system it had licensed from Arbutus – and then refused to reveal the details concerning its new "proprietary" system).

[70] Noah Higgins-Dunn, "Moderna Ceo Says He's Not Losing Any Sleep over Biden's Support for Covid-19 Vaccine Waiver," *Fierce Pharma* (2021), https://www.fiercepharma.com/pharma/moderna-ceo-says-he-s-not-losing-any-sleep-over-biden-s-endorsement-for-covid-19-ip-waiver.

The net result is that, even in the many countries in which the firms had not obtained (or even sought) patents, they were unlikely to face competition.

In the end, two of the three mRNA vaccines proved both safe and remarkably effective. The BioNTech/Pfizer product received an emergency use authorization by the FDA on December 11, 2020; the Moderna product did so a week later. Approvals by the EMA followed shortly thereafter. Distribution of both products in developed countries began immediately. (Clinical trials of the CureVac product were less successful, and it was never launched.)

Meanwhile, other companies had been using more traditional technologies to develop COVID vaccines. Johnson & Johnson's product received an EUA a few months after the mRNA entrants. Unfortunately, concerns about possible adverse side effects prompted the FDA and CDC to "pause" their endorsements of it. Those concerns were soon addressed and the pause ended,[71] but the J&J product never recovered commercially. By contrast, several other traditional vaccines stood the test of time. Among them were those by Sinovac and Sinopharm (distributed primarily in China), Gamaleya Research Institute (distributed primarily in Russia), Bharat Biotech and the Indian Council of Medical Research (distributed primarily in India), and, last but not least, AstraZeneca and Oxford University (distributed throughout the world).[72] None of these traditional vaccines, however, matched the mRNA vaccines in demonstrated effectiveness.

Running parallel to the race to develop vaccines was a similar race to find therapeutic drugs that, when given to people who have contracted the virus, could mitigate symptoms and reduce the risk of death. Some of the therapeutics consisted of applications or adaptations of existing treatments for other diseases; others were new. They varied widely in effectiveness. For a while, it appeared that remdesivir, developed previously by Gilead as a remedy for Ebola, would be also effective against COVID, but its benefits proved modest. The drugs that eventually proved most efficacious were three antivirals (Paxlovid, developed by Pfizer; Lagevrio, by Merck; and Xocova, by Shionogi) and four monoclonal antibodies (Bebtelovimab and Bamlanivirmab, developed by Lilly; Xevudy, by GSK and Vir; and REGEN-COV, by Regeneron and Roche).[73]

The developers of the therapeutics used a similar set of shields to augment their ability to control prices. Like the creators of the vaccines, they sought and obtained patents, both on the APIs and on supporting technologies, in many jurisdictions. The result was a

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[71] See "FDA and CDC Lift Recommended Pause on Johnson & Johnson (Janssen) COVID-19 Vaccine Use Following Thorough Safety Review," April 23, 2021, https://www.fda.gov/news-events/press-announcements/fda-and-cdc-lift-recommended-pause-johnson-johnson-janssen-covid-19-vaccine-use-following-thorough.

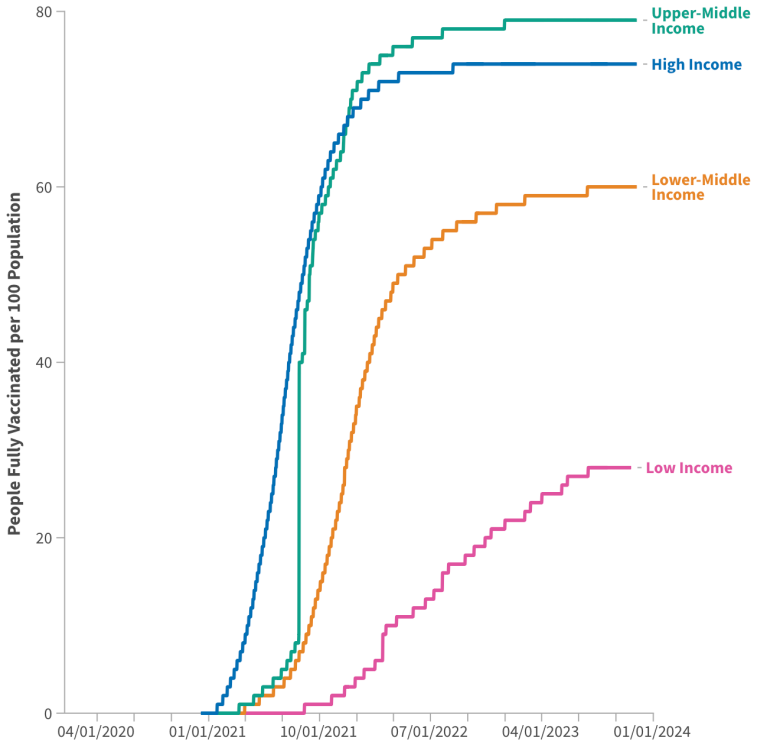
[72] For data concerning the total production of these vaccines (as of January 2022), see Policy, "Covid-19 Vaccine Production."

[73] See US International Trade Commission, "Covid-19 Diagnostics and Therapeutics: Supply, Demand, and Trips Agreement Flexibilities," (2023), 107, 12.; FDA, "Coronavirus (COVID-19) Drugs," https://www.fda.gov/drugs/emergency-preparedness-drugs/coronavirus-covid-19-drugs (last visited January 13, 2025).

formidable hedge of exclusive rights analogous to the hedge that shielded the vaccines.[74] In addition, limits on access to proprietary know-how provided powerful protection against competitors. This was especially true with respect to the monoclonal antibodies, which are far more difficult to reverse engineer than the small-molecule antivirals.[75] As was the case with vaccines, the firms that developed the therapeutics sometimes contested each other's rights – and sometimes instead collaborated.[76]

As Chapter 2 explained, both the vaccines and the therapies were initially distributed primarily in developed countries. The delay in their availability in poor countries is shown below.

Figure 9: Vaccination Rates by Income Group[77]



As these gaps became increasingly glaring, criticism of the firms intensified. Public-health advocates sought ways to provoke, help, or compel them to make their products available more widely.[78] Among their initiatives was the COVID-19 Technology

[74] See Mengru Lyu et al., "The Global Patent Landscape of Mrna for Diagnosis and Therapy," *Nature biotechnology* 41, no. 9 (2023); Commission, "Covid-19 Diagnostics and Therapeutics," 71-72.

[75] See "Covid-19 Diagnostics and Therapeutics," 74.

[76] See ibid., 178-82.

[77] Source: UNDP, "Global Dashboard for Vaccine Equity," (2024).

[78] See, e.g., "Who's Tedros Says Covid-19 Vaccine Inequity Creates 'Two-Track Pandemic'," *Reuters* (2021), https://www.reuters.com/business/healthcare-pharmaceuticals/whos-tedros-says-covid-19-vaccine-inequity-creates-two-track-pandemic-2021-06-07/; J. Peter Figueroa et al., "Urgent Needs of Low-Income

Access Pool (C-TAP), created in May of 2020 by the World Health Organization in collaboration with the government of Costa Rica. The Pool is similar to the MPP in that it solicits contributions (in the form of nonexclusive voluntary licenses) of intellectual property and know-how – and then issues sub-licenses to other companies and institutions. Its primary difference from the MPP pertains to the scope of the licenses; all are global in their coverage. C-TAP enjoyed considerable support. 44 other countries quickly endorsed it, and its partners include the UNDP, Unitaid, the UN Technology Bank, and the MPP.[79]

For the most part, the firms were unresponsive to the pleas of the public-health advocates. This was especially true of the companies that had developed the mRNA vaccines. To be sure, in response to criticism, Moderna pledged not to "enforce our COVID-19 related patents against those making vaccines intended to combat the pandemic."[80] However, as the comment by Mr. Bancel quoted above makes clear, this was a hollow promise. In the absence of technology transfer and regulatory support, no other company would have been able to make and distribute a replica of the Moderna vaccine within a reasonable period of time.[81]

The best indicator of the posture of the firms was their response to the formation of C-TAP. During its first three year, only two organizations (the Spanish National Research Council and the U.S. National Institutes of Health) issued licenses through the C-TAP,[82] and only one company (Biotech Africa) obtained a sublicense (specifically, on a COVID

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and Middle-Income Countries for Covid-19 Vaccines and Therapeutics," *The Lancet (British edition)* 397, no. 10274 (2021); Carlos Correa, "Expanding the Production of Covid-19 Vaccines to Reach Developing Countries: Lift the Barriers to Fight the Pandemic in the Global South," (South Centre, 2021); Peter Loftus, "Pfizer, Moderna and J&J Face Shareholder Pressure to Broaden Covid-19 Vaccine Access," *Wall Street Journal*, March 22, 2022 2022; Siva Thambisetty et al., "Addressing Vaccine Inequity during the Covid-19 Pandemic: The Trips Intellectual Property Waiver Proposal and Beyond," *Cambridge law journal* 81, no. 2 (2022); Editorial Board, "The World Needs Many More Coronavirus Vaccines," *New York Times*, April 24, 2021.

[79] See https://www.who.int/initiatives/covid-19-technology-access-pool.

[80] Moderna, "Statement by Moderna on Intellectual Property Matters during the Covid-19 Pandemic," news release, October 8, 2020, 2020, https://perma.cc/R9VB-2ULH.

[81] In 2021, Martin Friede, the leader of the vaccine research initiative at the World Health Organization, estimated that, in the absence of technology transfer from Moderna, it would take Afrigen, a sophisticated biotech firm, "from three or four years" to replicate the Moderna vaccine. See Nurith Aizenman, "Moderna Won't Share Its Vaccine Recipe. Who Has Hired an African Startup to Crack It," *Nationa Public Radio* (2021), https://www.npr.org/sections/goatsandsoda/2021/10/19/1047411856/the-great-vaccine-bake-off-has-begun. That prediction proved remarkably accurate.

[82] The license by the former is available at https://www.who.int/initiatives/covid-19-technology-access-pool/csic-license. The license by the latter is available at https://www.who.int/initiatives/covid-19-technology-access-pool/us-nih-licenses. The NIH's own summary of their contributions is available at https://www.techtransfer.nih.gov/policy/ctap. The resistance by all other potential licensors is described in Ed Silverman, "Pharma leaders shoot down WHO voluntary pool for patent rights on Covid-19 products," STAT, May 28, 2020, https://www.statnews.com/pharmalot/2020/05/28/who-voluntary-pool-patents-pfizer/.

diagnostic test).[83] Not until August of 2023 (when the pandemic was effectively finished) was a vaccine candidate licensed through the system.[84]

The center ring for the prolonged struggle between the companies and the public-health advocates was a multi-year effort to secure from the World Trade Organization a "waiver" of the provisions of the TRIPS Agreement that curtailed countries' ability to overcome the companies' shields. That effort was initiated by the governments of India and South Africa. In October of 2020, they requested "a waiver from the implementation, application and enforcement of Sections 1, 4, 5, and 7 of Part II of the TRIPS Agreement in relation to prevention, containment or treatment of COVID-19." They asked that the waiver remain in place "until widespread vaccination is in place globally, and the majority of the world's population has developed immunity."[85] After seven months of fraught negotiations, both public and private, the United States announced (to the surprise of most observers) that it could support some kind of waiver "for COVID vaccines."[86] India and South Africa, now with the support of many other developing countries, then proposed a waiver only slightly narrower than their original version. Unlike the statement by the U.S., the revised proposal encompassed, not just vaccines, but all "health products and technologies including diagnostics, therapeutics, vaccines, medical devices, personal protective equipment, their materials or components, and their methods and means of manufacture for the prevention, treatment or containment of COVID-19."[87] Soon thereafter, the European Union, apparently unmoved by the temperate stance taken by the U.S., offered an extremely narrow accommodation of the request by the developing countries. The EU proposal merely acknowledged that the COVID pandemic constitutes a "circumstance of extreme urgency" within the meaning of Articles 31 and 31bis and loosened slightly the requirements with which countries must abide when issuing compulsory licenses applicable to patents on vaccines and medicines aimed at COVID.[88]

After yet another year of negotiations, the Ministerial Conference of the WTO finally announced a clarification of the TRIPS Agreement nearly as circumscribed as the

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[83] See https://cdn.who.int/media/docs/default-source/medicines/c-tap/sublicence-agreement-mpp-biotech-africa.pdf?sfvrsn=59cc142e_1. ; "New C-TAP agreement aims to improve global access to COVID-19 testing technologies," June 16, 2022, https://www.who.int/news/item/16-06-2022-new-agreement-under-c-tap-aims-to-improve-global-access-to-covid-19-testing-technologies

[84] See WHO, "Who Initiative Signs New Licensing Agreements on Covid-19 Technologies," news release, August 29, 2023, 2023, https://perma.cc/3477-5SQF; Priya Venkatesan, "New Licences for the Covid-19 Technology Access Pool," *The Lancet. Microbe* 4, no. 12 (2023).

[85] World Trade Organization, "Communication from India and South Africa: Waiver from Certain Provisions of the Trips Agreement for the Prevention, Containment and Treatment of Covid-19," (2020).

[86] United States Trade Representative, "Statement from Ambassador Katherine Tai on the Covid-19 Trips Waiver," news release, May 5, 2021, 2021, https://perma.cc/JN53-Y5UW.

[87] World Trade Organization, "Communication from the African Group, the Plurinational State of Bolivia, Egypt, Eswatini, Fiji, India, Indonesia, Kenya, the Ldc Group, Maldives, Mozambique, Mongolia, Namibia, Pakistan, South Africa, Vanuatu, the Bolivarian Republic of Venezuela and Zimbabwe: Waiver from Certain Provisions of the Trips Agreement for the Prevention, Containment and Treatment of Covid-19," (2021).

[88] "Communication from the European Union to the Council for Trips: Draft General Council Declaration on the Trips Agreement and Public Health in the Circumstances of a Pandemic," (2021).

one advocated by the EU. It was limited to vaccines, applied only "to the extent necessary to address the COVID-19 pandemic," was available only to self-declared "developing countries," and, rather than "waiving" the limits imposed by TRIPS upon countries' authority to issue compulsory licenses, loosened only modestly the procedural and substantive requirements with which they had to abide.[89]

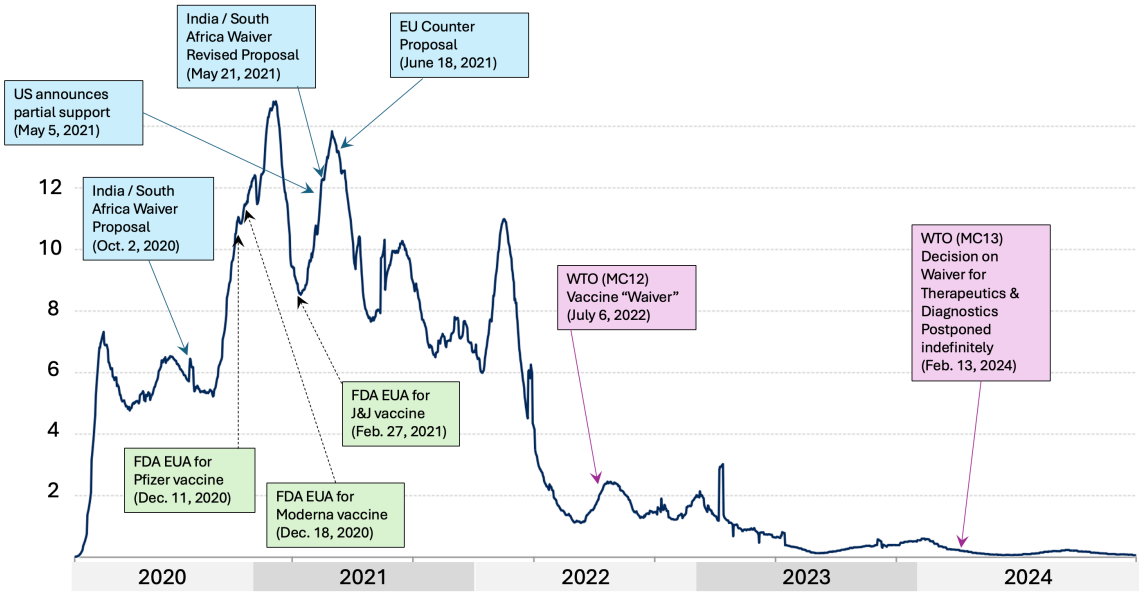
The 2022 Decision left open the question of whether the partial suspension of TRIPS would be "extended" from vaccines to COVID therapeutics and diagnostics. After 20 months of additional discussions and negotiations (in which one of the authors played a minor role) and the publication of a comprehensive report by the US Trade Commission, the Ministerial Conference decided not to resolve the issue – in effect postponing an answer to the question forever.[90]

For three independent reasons, neither of decisions by the WTO Ministerial Conference had any material direct effect on the availability of COVID vaccines or therapeutics. First, as we have seen, only the first of the two rulings modified in any way the constraints imposed by TRIPS – and its ambit was narrow. Second, even generous waivers of the TRIPS constraints would have weakened only one of the shields the firms used to suppress competition – namely, their patent portfolios. All of the other shields would have remained intact. Third, as the timeline set forth below shows, by the time the WTO issued its rulings, the pandemic had largely subsided.

[89] "Ministerial Decision on the Trips Agreement," (Ministerial Conference, Twelfth Session, 2022).

[90] For some of the contributions to the prolonged debate over what came to be known, inaccurately as the "waiver extension," see American Federation of Teachers et al., "Please Extend the Wto Trips Decision to Treatments and Tests and Support Countries Using Wto Flexibilities to Access Covid-19-Related Medical Technologies," (2022); European Federation of Pharmaceutical Industries and Associations, "A Fact-Based Analysis of the Trips Waiver Extension," (2022); World Trade Organization, "Council for Trips Paragraph 8 of the Ministerial Decision on the Trips Agreement: Informal Thematic Session for External Stakeholder Input, Report by the Chair," (2024). The decision itself in available at "Paragraph 8 of the Ministerial Decision on the Trips Agreement Adopted on 17 June 2022: Report to the General Council," (2024).

Figure 10: The COVID Waiver Debate Juxtaposed to Global Deaths[91]



This is not to say, however, that the controversy over the "COVID waiver" was entirely a sideshow. By helping to sustain public awareness of the plight of developing countries, the debate added significantly to the pressure on the firms to find some alternative way of reducing global inequity in access to their products.

The principal response of the developers of the vaccines was to enter into contracts with a few companies located in low-income or middle-income countries to manufacture branded versions of their products. For example, in July of 2021, Pfizer and BioNTech contracted with Biovac, a South African biopharmaceutical company, to produce the Pfizer vaccine in its Cape Town facility. The deal contemplated that "manufacturing of finished doses will commence in 2022. At full operational capacity, the annual production will exceed 100 million finished doses annually. All doses will exclusively be distributed within the 55 member states that make up the African Union."[92] AstraZeneca entered into similar

[91] The reason for the exclusion of China and South Korea from the representation of global deaths is not that those countries are unimportant, but rather that the long delays between deaths in those countries and the time at which those deaths were reported produces a distorted picture of the progress of the pandemic.

[92] Pfizer, "Pfizer and Biontech Announce Collaboration with Biovac to Manufacture and Distribute Covid-19 Vaccine Doses within Africa," news release, July 21, 2021, 2021, https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-announce-collaboration-biovac. The tone of the press release made clear the extent to which the deal was provoked by criticism of the company in the previous year: "From day one, our goal has been to provide fair and equitable access of the Pfizer-BioNTech COVID-19 Vaccine to everyone, everywhere," said Albert Bourla, Chairman and Chief Executive Officer, Pfizer. "Our latest collaboration with Biovac is a shining example of the tireless work being done, in this instance to benefit Africa. We will continue to explore and pursue opportunities to bring new partners into our supply chain network, including in Latin America, to further accelerate access of COVID-19 vaccines."

contracts with Serum Institute in India and Fiocruz in Brazil.[93] These were not voluntary licenses in the special sense in which that term is now conventionally used. Rather, they were traditional manufacturing contracts for the production and distribution of branded versions of the vaccines at issue. The output of products through these channels was substantial, but did not begin to reach most poor countries until roughly a year and a half after the vaccines were being widely distributed in rich countries.

The developers of the therapeutics, by contrast, began to employ voluntary licenses of the sort that had been developed and refined in the context of HIV and HCV. The principal terms of the most important licenses they granted are set forth (in chronological order) in the following table.[94]

Figure 11: Voluntary Licenses for COVID Therapeutics

Licensor	Drug	Date	Mode	Countries	Licensees
Gilead	remdesivir	May 2020	bilateral	127	9
Merck	molnupiravir	April 2021	bilateral	106	8
Lilly	baricitinib	May 2021	bilateral	?	8
Merck	Molnupiravir (Lagevrio)	October 2021	MPP	106	27
Pfizer	Nirmatrelvir + ritonavir (Paxlovid)	November 2021	MPP	95	38
Shionogi	Ensitrelvir (Xocova)	October 2022	MPP	117	7

In most respects, these licenses mirrored the voluntary licenses pertaining to HIV and HCV. Each authorized the licensees to produce and to distribute, within the specified countries, generic versions of the licensor's products. The licensees were free to set the prices for their products. Typically, the licensor promised to assist the licensees in various ways – most importantly by disclosing proprietary know-how to facilitate manufacturing, but also by providing various forms of assistance in obtaining regulatory approval. Most provided that royalties would be waived altogether during the pandemic and would remain modest thereafter – typically 5% of sales.

[93] See Thambisetty et al., "Addressing Vaccine Inequity during the Covid-19 Pandemic: The Trips Intellectual Property Waiver Proposal and Beyond." The Fiocruz contract is available at Fiocruz, "Technological Order Agreement Entered into by Fundacao Oswaldo Cruz — Fiocruz, Instituto De Tecnologia Em Imunobiologicos — Bio-Manguinhos and Astrazeneca Uk, Ltd.," (2020).

[94] The information contained in this table has been assembled from MPP, "Accelerating Access through Community Partnership: Annual Report 2023," (2024); Commission, "Covid-19 Diagnostics and Therapeutics."; Chenglin Liu, "Beyond Compulsory Licensing: Pfizer Shares Its Covid-19 Medicines with the Patent Pool," *Legislation and Public Policy* 25 (2021); Morgan Pincombe and Javier Guzman, "Lessons from Expanding Access to Covid-19 Treatments in Lmics through Voluntary Licensing," (Center for Global Development, 2022).

On paper, these licenses were and are impressive. Unfortunately, in practice their contribution to the mitigation of the pandemic was modest. One of the factors that limited their impact was their modest geographic scope. The broadest in coverage was the Gilead license for remdesivir, but unfortunately that drug proved less effective than the other therapeutics. The licenses to the other drugs on the list typically excluded large upper-middle-income countries that the firms regarded as significant potential sources of revenue. Among the countries left out of all of the licenses (other than Gilead's) are Mexico, Brazil, Chile, Argentina, Turkey, and China.

Even more important than this geographic limitation was the constraint imposed by the timing of the licenses. By the time they were issued, the pandemic was already starting to fade. Most of the licensees, recognizing that building their manufacturing capacity and securing regulatory approvals for their products would take many months, never even started those processes.[95] For example, as of the end of 2023, only 7 of the 27 sublicenses issued by the MPP for molnupiravir were "active," and most of the licensees were still awaiting regulatory approval. Similarly, only 12 of the MPP sublicenses for nirmatrelvir/ritonavir were "active," and only 4 of those licensees had received WHO prequalification approval.[96]

The licenses surely did some good. The MPP reports that, but the end of 2023, 606,000 courses of molnupiravir had been supplied in India and Guatemala, and 76,000 courses of nirmatrelvir/ritonavir had been supplied in 13 low-income and lower-middle-income countries.[97] But by that time, there had been roughly 750 million confirmed COVID cases in the world. The number of therapeutic treatments enabled by the MPP voluntary licenses represents 0.09% of that total. In sum, for the most part, the fruits of the voluntary licenses for COVID therapeutics must be considered too little, too late.

B. Guidelines

One of the reasons for the growing popularity of the strategy of voluntary licensing is that it seems to provide a way of pleasing everyone. Like differential pricing, discussed in the preceding chapter, voluntary licensing is often described as a "win-win" solution to the global health crisis. Upon closer examination, however, it becomes apparent that the interests of the parties with stakes in a voluntary license are not identical. The present section begins by mapping those interests. It then offers a set of guidelines, distilled from the history of this approach, that could maximize opportunities for reconciling those interests and thereby increase the usage and benefits of this strategy.

By agreeing to a voluntary license of the sort exemplified by the HIV, HCV, and COVID contracts detailed above, a pharmaceutical firm stands to benefit in seven

[95] See Commission, "Covid-19 Diagnostics and Therapeutics," 191.

[96] See MPP, "Annual Report 2023," 51.

[97] See ibid.

intertwined ways. First, it can earn revenue in the form of royalties. As we have seen, those royalties are customarily set at low levels. But, because the expenses associated with the licenses are modest, the royalties are usually sufficient to provide the firm a profit.

Second, a voluntary license can help the firm "shape the market" in the countries included in the footprint of the license, thereby enabling the firm to earn more substantial profits in the future. A recent report prepared by the MPP described this opportunity as follows:

> [M]arket shaping is … the preparation of a market that facilitates future entry of a follow-on medicine. Preparation of a market includes: (i) advocacy and education of healthcare professionals and affected communities; (ii) government advocacy; (iii) creation of budget lines; (iv) creation of infrastructure to diagnose and treat the disease.[98]

The MPP argues, plausibly, that by using a voluntary license to facilitate deployment of generic versions of a product in a poor country, a firm can in these ways prepare the ground for subsequent, more lucrative sales of branded second-generation products.

Third, the firm can reap an additional benefit in the form of good public relations. As Chapter 4 discussed, this is an increasingly important area of concern for pharmaceutical companies.

Fourth, for related reasons, a firm using a voluntary license to aid developing countries may find it easier to retain researchers and other skilled employees, many of whom are public-spirited, at least to some degree. That, in turn, reduces the cost to the firm of recruiting and training new employees.[99]

Fifth, a track record of promoting public health in developing countries may help the firm obtain financing on more favorable terms than would otherwise be available. So-called "sustainability-linked bonds," bearing lower-than-usual interest obligations or other beneficial features contingent upon achievement of social-welfare goals, are already being issued by some pharmaceutical firms, and their use may become more common soon.[100]

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[98] MPP, "Voluntary Licensing: Right for Health," 19.

[99] See ibid.

[100] For discussion of sustainability-linked bonds in general (and the associated hazard of "greenwashing"), see World Economic Forum, "What Are Sustainability Linked Bonds and How Can They Support the Net-Zero Transition?," (2022); Frederic de Mariz et al., "Reforming Sustainability-Linked Bonds by Strengthening Investor Trust," *Journal of risk and financial management* 17, no. 7 (2024); Anne-Marie Anderson and Richard Kish, "Rewarding Performance through Sustainability-Linked Bonds," *Economic affairs (Harlow)* 44, no. 2 (2024); Diana Sellevold and Philip Larsen, "Sustainability-Linked Bonds an Examination of Yield Differences between Sustainability-Linked and Conventional Bonds" (OsloMet-Storbyuniversitetet, 2023). For discussion of their actual or potential use by pharmaceutical firms, see Gore et al., "Negotiating License Agreements," 4.; MPP, "Voluntary Licensing: Right for Health," 30.

Sixth, by making generic versions of a product available at a low price in poor countries instead of distributing a branded version of the product at the same price in those countries, the firm avoids the risk discussed in the preceding chapter – namely, that application of the "referencing pricing" systems used in some wealthy countries will punish the firm for its altruism.[101]

Last but not least, if (for the reasons discussed in Chapter 4) the executives of the firm aspire among other things to save lives, voluntary licensing offers them a way to do so. Plainly, demonstrations of the firm's commitment to save as many lives as possible underpins several of the more prosaic benefits just itemized. This seventh benefit contemplates, optimistically, that the firm's leaders are convinced that they have moral obligations to promote the welfare of the global poor – i.e., obligations not reducible to augmentation of the firm's bottom line.

On the other side of the ledger, voluntary licensing carries with it some risks to the firm, which its executives would like to minimize. The most important of those hazards are corrosion of the markets for the firm's products in wealthier countries and loss of control over proprietary technologies.

The second of the constituencies whose interests must be considered is the set of generic manufacturers to whom a voluntary license is granted. The active participation of the licensees is essential to the success of a voluntary license. Thus, it is crucial that the deal be structured to address the licensees' concerns as well as those of the licensor.

Like the licensor, each licensee wishes to make a profit. Unless the licensees' executives see a path to making money, they will not invest the funds necessary to build capacity and secure approval for the authorized products. As we saw, the obscurity of such a path was one of the main reasons that the voluntary licenses for COVID therapeutics had so little impact.

The executives of potential licensees are also interested in augmenting their firms' technological capacities, which will enhance ability of the firms to take on similar or more complex projects in the future.

Last but not least, the licensees' executives are usually interested in establishing and maintaining long-term relationships with innovator pharmaceutical firms, in part because those relationships make future lucrative deals more likely.

Although typically the nations identified in a voluntary license are not formally parties to the deal, in practice their cooperation is also essential to success. Thus, their interests must be accommodated as well. More specifically, the deal must take into account the views and desires of the leaders of those countries.

[101] See pages ____, above.

The most obvious of the leaders' interests is to minimize the prices of the vaccine or therapeutic addressed by the license, thereby enabling the leaders to maximize the number of the nation's residents who benefit. In addition, the leaders of many countries now wish to incorporate in all voluntary licenses provisions for "local production" of the vaccine or therapeutic at issue. To appreciate the strength and importance of the latter commitment requires a bit of background.

For many years, most of the pharmaceutical products distributed and consumed in poor countries have been manufactured either in upper-income countries or in large middle-income countries (primarily India, China, and Brazil). For decades, lawmakers and activists seeking to improve health conditions in poor countries have debated the wisdom of altering this situation – in other words, increasing the amounts and percentages of drugs that are manufactured locally. Advocates of augmenting local production contend that it would benefit the residents of poor countries in two ways. First, it would create many high-paying skilled jobs and would support sustainable economic development. Second, local firms could respond more quickly to the residents' changing health needs. Skeptics have responded that local production, by forfeiting economies of scale, would be less efficient and thus would raise the costs of medicines. In addition, the skeptics contend that the systems for maintaining the quality of drugs are less robust in developing countries, and thus that local production would lead to an increase in SFMPs.[102]

The relative salience of these competing clusters of arguments have been altered by the behavior of national governments and pharmaceutical companies during the COVID-19 pandemic. As we have seen, most governments when managing scarce supplies of products capable of curbing the disease (protective equipment and diagnostics, as well as vaccines and therapeutics) gave strong preference to their own citizens or residents.[103] Because (a) most of those products were produced in either upper-income or upper-middle-income countries and (b) the companies producing them either actively supported the governments' policies or acquiesced, the lion's shares of all the most effective products ended up in rich countries. The disparity resulted in many unnecessary deaths.[104]

There is no reason to suppose that either governments or companies will behave differently when they are faced with the next pandemic. Thus, if we wish not to replicate

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[102] *Compare* Frederick Abbott and Jerome H. Reichman, "The Doha Round's Public Health Legacy: Strategies for the Production and Diffusion of Patented Medicines under the Amended Trips Provisions," *Journal of International Economic Law* 10, no. 4 (2007). with Roger Bate, "Local Pharmaceutical Production in Developing Countries: How Economic Protectionism Undermines Access to Quality Medicines," (2008); Warren Kaplan and Richard Laing, "Local Production of Pharmaceuticals: Industrial Policy and Access to Medicines," *HNO Discussion Paper 32036* (2005).

[103] See, e.g., Vishnu Som, "Indian Vaccine Export Ban Makes 91 Nations Vulnerable to New Strains: WHO," NDTV, May 31, 2021, https://www.ndtv.com/india-news/indian-vaccine-export-ban-makes-91-nations-vulnerable-to-new-strains-who-2453195; https://www.bloomberg.com/news/articles/2021-05-03/white-house-backs-pfizer-s-move-to-begin-u-s-vaccine-exports#xj4y7vzkg.

[104] See, e.g., Sam Moore et al., "Retrospectively Modeling the Effects of Increased Global Vaccine Sharing on the Covid-19 Pandemic," *Nature Medicine* 28 (2022).

the inequity of COVID-19, we need to find ways to increase production capacity in poor countries.

The leaders of most poor countries have now fully accepted the foregoing proposition – as have the relevant intermediaries.[105] Not all of the executives of pharmaceutical firms are yet convinced. However, if they wish a voluntary license to work, they will need to accommodate the views of the national leaders. As illustrated by several of the stories in the first half of this chapter – and as will become increasingly apparent in the discussion below – cooperation by the leaders of a country to which such a license applies is often critical to its success. The upshot is that, even licensors who remain skeptical of local production will be obliged in the future to accommodate the leaders' view on this score.

For a subset of voluntary licenses, there is one more interested party whose interests merit attention. As we have seen, some voluntary licenses are negotiated through and administered by intermediaries. Currently, the Medicines Patent Pool is by far the most important of those intermediaries, but occasionally other organizations serve this function. Examples include the Clinton Health Initiative and C-TAP. These intermediaries are not neutral brokers; they have interests of their own.

A minor but not trivial interest is staying in business. The leaders of the intermediaries, like the leaders of almost all organizations, wish to justify the services they provide and thus to maintain or augment their positions in the pharmaceutical ecosystem.

More important for present purposes is the philanthropic interest of the intermediaries. The MPP, in particular, was created by UNITAID for a purpose: to increase the availability of medicines and thus promote global public health. Its leaders, to their credit, consistently pursue that goal. That means, among other things, that when negotiating licenses, the leaders of the MPP strive to include terms that will maximize the benefits (long term as well as short term) reaped by the residents of both low-income and middle-income countries. In this sense, the MPP works to shield the interests of the global public at large, which otherwise would not have a seat at the table where a deal is done.

As is likely already apparent, the interests of these four constituencies – licensors, licensees, affected nations, and intermediaries – overlap to a large extent, certainly enough to make voluntary licenses possible. However, they do not align perfectly. The balance of this section presents guidelines that could help reconcile them and thus increase the willingness of all parties to employ this strategy. We begin with some topics where accommodation of partially divergent interests is relatively easy and proceed to topics where reconciliation has been (or could be) more difficult.

[105] See, e.g., United Nations. Economic Commission for Africa; United Nations Economic Commission for Africa (2020-06). Africa's Response to COVID-19: what roles for trade, manufacturing, and intellectual property? Addis Ababa. © UN. ECA. https://repository.uneca.org/handle/10855/43761.

1. Timing

All parties benefit when a voluntary license is adopted and implemented as early as possible in the fight against a disease – ideally, even before the drug in question has received regulatory approval in developed countries. The window in which the licensees can earn a profit is maximized by such early intervention, as is the licensor's revenue from royalties. In addition, the licensor reaps public-relations benefits from taking the initiative, which are greater than when the company' response appears grudging. The intermediary gets appropriate credit for facilitating an early deal. Last but not least, the number of people in the nations covered by the license who benefit from access to the drug is increased.

The benefits of early action are apparent from the fruits of the deployment of generic Sovaldi in Egypt. The costs of delay are apparent from the history of COVID vaccines and therapeutics.

2. Selectivity

It is sometimes feasible for a licensor to surrender control over the number and identities of the manufacturers who are authorized to produce generic versions of a product. However, retention and exercise of such control has three potential advantages for the licensor. First, it enables the licensor to provide access to its technology only to generic manufacturers that it trusts – and specifically, is confident will adhere to quality-control standards, respect trade secrets, and work assiduously to prevent the diversion of products to upper-income countries. Second, each licensee's desire to remain among the set of trusted partners – and thus to be a candidate for future deals with the licensor – augments the licensee's incentive to behave responsibly. This is particularly important in connection with new, important products that represent potential platforms. Third, retention of control enables the licensor to control the number of manufacturers who are competing to sell generic versions of the product in each LMIC market.

The third of these advantages is not obvious. Why would the licensor want to limit competition? Saving as many lives as possible (and reaping all of the associated advantages) would seem to counsel maximizing competition among licensees, because it would most effectively reduce the prices of the generics in each market. Although that consideration deserves considerable weight, it is partially offset by several benefits of curbing competition enough to ensure that each licensee is able to earn a normal profit: It reduces the incentive of each licensee to skimp on quality control to cut costs; it increases the incentive of each licensee to work actively to secure local regulatory approval for the drug as soon as possible; and it helps to build the capacities of generic manufacturers, which is beneficial in the long run.[106]

Plainly, these considerations also advance the interests of the licensees who are included in the fold. Because the same considerations increase the likelihood that the deal

[106] See Baker, "Sliver of Hope."

will produce widespread availability of low-cost, high-quality drugs, they advance the interests of all other parties as well.

The strength of these factors will vary by context. In determining an appropriate number of licensees, the licensor should consider:

- the size of the relevant market, based upon the size of the population and the prevalence of the disease at issue;
- the likely duration of the market, which in turn will be heavily affected by whether the drug at issue is capable of eradicating the disease (like the HCV drugs) or only managing it (like the HIV drugs);
- the cost to each licensee of setting up a manufacturing line for the drug;
- the ease with which the manufacturing facility could be adapted by the licensee to other products in the future; and
- the track record of each potential licensee, which will help in predicting the likelihood that it will prove incapable of commencing or continuing production.

When building a cadre of authorized manufacturers, both licensors and licensees should be mindful of the advantages of long-term, rather than one-off commercial relationships. Ideally, the licensor should select a set of licensees with whom it hopes to collaborate with respect to the manufacture and distribution of a series of products, rather than a single drug. Such relationships build trust and reduce transaction costs – and may reduce manufacturing costs.

Finally, the licensor should consider subdividing the market vertically. Specifically, it may sometimes be optimal to enter into some licenses exclusively for the active pharmaceutical ingredient (API), so that all of the licensees producing finished goods can access that API. If one of the finished-goods manufacturers also controls the supply of the API, then that manufacturer can raise API prices to the other licensees to advantage its own finished product. Also, manufacturers that are adept at manufacturing the finished product but unable to produce the API might not enter into a voluntary license if the API is not available through another channel. Thus, having a separate license for an API-only producer can expand the cohort of potential licensees producing the finished product.

3. Technology Transfer

Because traditional "small-molecule" drugs can be reverse engineered easily by modern generic manufacturers, it may not be essential for licenses pertaining to those drugs to be accompanied by agreements to make proprietary know-how available to the licensees. This is not true, however, of drugs founded upon more complex technologies, such as biologics and mRNA-based vaccines. Even when it is possible for licensees to reverse engineer such products, forcing them to do so is highly inefficient. The drugs at issue will be delivered to the populations of the affected countries faster and less expensively if a licensor commits to transfer relevant technology to the licensees.

To be sure, the trade secrets associated with complex drugs are often extremely valuable, and pharmaceutical firms understandably fear that making them available to licensees could cause them to escape "into the wild." But refusing to transfer technology is an unnecessary and ultimately ineffective way of avoiding that hazard. Instead, licensors can and should employ some of the protective strategies already mentioned – such as issuing licenses only to trusted partners and then giving those licensees incentives to be scrupulous in preventing breaches of confidentiality.

Benefits to all parties are also generated by transfers of technology in the opposite direction. Generic companies operating under voluntary licenses often develop cheaper or more reliable ways of manufacturing the drugs at issue than were known to the innovators. In addition, they sometimes develop new products based on the patents or knowhow transferred. "Grantback" provisions in VLs require the licensees to reveal and license such discoveries to the innovator at no cost and with the right to manufacture and sell those improvements.

To maximize each licensee's incentive to develop such improvements, the grantback provisions may include a promise by the licensor not to provide the technology at issue to the other licensees without permission. To be sure, such a promise may forfeit some amount of manufacturing efficiency – if the licensee responsible for a refinement refuses to license it to the other members of the cadre of licensees. But a promise of this sort has the merit of accelerating the development of improvements and of more closely aligning the interests of each licensee with those of the licensor.

4. Quality Control

As Chapter 2 explained, substandard or falsified medical products [SFMPs] are distressingly common in pharmaceutical markets, especially those of low and middle-income countries.[107] Serious consequences result when SFMPs are purchased and consumed by unsuspecting patients. Most obviously, the consumers receive either zero or reduced therapeutic or immunological benefit. Consumers in imminent peril, such as young children who have contracted malaria, are likely to die before the reason they are not recovering becomes apparent. The long-term secondary effects of SFMPs are also serious. In many LMICs, faith in western medicine is weak and fragile. When what appear to be legitimate drugs do no good (or worse, cause harm), that faith corrodes. The result, of course, is to reduce the inclination of people who contract diseases to seek professional help. Equally important, the consumption of products containing less than the proper quantity of active ingredient contributes to the spread of drug-resistant variants of many diseases, which poses an increasingly dangerous threat to global health. The pharmaceutical firms selling authentic versions of the drugs at issue also suffer. Some of their potential sales are displaced by substandard or counterfeit products. More

[107] See Sachiko Ozawa et al., "Prevalence and Estimated Economic Burden of Substandard and Falsified Medicines in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis," *JAMA Network Open* 1, no. 4 (2018); WHO, "A Study of the Public Health and Socioeconomic Impact of Substandard and Falsified Medical Products," (2017).

importantly, the reputations of the drugs and of the companies from which they purportedly emanate are damaged. As the founder of one major firm aptly observed, "the pharmaceutical firm will own every disaster associated with its licensees." Finally, in cases in which SFMPs are purchased by public-health services, the result is a waste of the countries' scarce financial resources, which in turn either drains the government's coffers or impairs their ability to address residents' needs.

In sum, all of the parties to a voluntary license have an interest in structuring the deal in ways that will reduce the threat of SFMPs. One way of doing so has already been mentioned: all extant voluntary licenses include stringent requirements concerning the quality of the goods manufactured by the licensees. Violation of those provisions typically results in immediate termination of the agreement. Such provisions are plainly desirable.

A second, less obvious way of minimizing SFMPs is to grant licenses only to reliable manufacturers. When a licensor negotiates a license directly, this concern does and should loom large. When a license is instead negotiated through the MPP, the licensor formally retains the right to veto any licensee and thus the capacity to exclude manufacturers that the licensor does not already have good reason to trust. In practice, however, the MPP licenses typically result in larger sets of licensees being admitted to the fold. Consequently, more weight is borne by the MPP to police the conduct of the licensees to ensure quality control. To date, the MPP seems to have fulfilled that responsibility well. There are few if any reports of poor-quality drugs produced by the manufacturers overseen by the pool.

Although necessary, precautions of these sorts are not sufficient. SFMPs can still appear in the distribution chain for the drug at issue in one of two ways. First, properly manufactured generics can lose potency if they are stored or transported improperly. Second, when pharmacies and other dispensers experience stockouts (a common phenomenon in LMICs), they often obtain substitutes from the black market, and some of those substitutes are routinely counterfeit.[108]

To reduce these dangers, a voluntary-licensing system can and should be accompanied by an effective mechanism for post-market surveillance. As Chapter 5 suggested, the ideal surveillance system would be a comprehensive global "track and trace" regime. However, until a regime of that sort is available, voluntary licenses could incorporate one of the existing mechanisms (also described in Chapter 5) for randomly testing drugs at various points in the distribution chain to verify their quality. None of those mechanisms is perfect, but the best of the bunch uses near-infrared [NIR] scanners to compare the spectral profiles of randomly sampled drugs to the spectral profiles of authenticated drugs.[109]

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[108] See Harparkash Kaur et al., "Fake Anti-Malarials: Start with the Facts," Malaria Journal 15, no. 86 (2016): 6.

[109] For descriptions and evaluations of NIR systems, see Nantasit Luangasanatip et al., "Implementation of Field Detection Devices for Antimalarial Quality Screening in Lao Pdr—a Cost-Effectiveness Analysis,"

To function optimally, a system of this sort would require a collaboration among four parties:

1) The licensor would set the quality standards, including appropriate tolerances.
2) Each licensee would then adhere to those standards. Equally important, each time the licensee prepared a new batch of the licensed compound, it would deliver to the operator of the NIR system an authenticated spectral profile corresponding to the batch.
3) The operator of the NIR system would then modify the spectral library to include the new profile and would then update (through the Internet) all of the portable NIR devices.
4) The relevant government agency in the LMIC (typically the Medicines and Poisons Board) would then instruct its inspectors to use the devices when taking periodic samples of the drugs in circulation.

In the near future, even better technologies for rapid, reliable testing of samples of drugs will undoubtedly appear. Thus, it would be prudent to draft a license agreement so that the licensee is not bound to employ any particular technology, but rather is free to use the one that is currently optimal. What's essential is that the agreement mandate deployment of some system of this sort.

5. Maximizing Impact

Plainly, a voluntary license will achieve its intended effect of maximizing the availability of the drug at issue only if the prices paid by patients are low. In the typical initiative, three of the parties with stakes in the deal have an incentive to keep prices low: the licensor, the government of the country to which the license pertains, and the intermediary, if any. Unfortunately, other players – most notably, the licensees, distributors, and retailers – may be more interested in maximizing their profits. Keeping their margins within reasonable bounds is crucial.

One familiar way of doing so would be for the government of each nation named in the license to regulate the price of the drug, either by capping the amount that may be charged at the retail level or by limiting the markups that may be made at each stage in the distribution chain. Many LMICs already maintain lists of drugs whose prices are

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PLOS Neglected Tropical Diseases 15, no. 9 (2021): 12-13.; P.H. Ciza et al., "Comparing the Qualitative Performances of Handheld Nir and Raman Spectrophotometers for the Detection of Falsified Pharmaceutical Products," *Talanta* 202 (2019): 477.; Wenbo Wang et al., "Evaluating Low-Cost Optical Spectrometers for the Detection of Simulated Substandard and Falsified Medicines," *Applied Spectroscopy* 74, no. 3 (2020): 332.; Stephanie Kovacs et al., "Technologies for Detecting Falsified and Substandard Drugs in Low and Middle-Income Countries," *PLoS ONE* 9, no. 3 (2014): 8, 10.; Moussa Yabré et al., "Detection of Falsified Antimalarial Sulfadoxine-Pyrimethamine and Dihydroartemisinin-Piperaquine Drugs Using a Low-Cost Handheld near-Infrared Spectrometer," *Journal of Analytical Methods in Chemistry* 2022 (2022): 6.

controlled in one of these ways;[110] these governments could readily add to their lists drugs that enters the market through voluntary licenses.

In practice, this strategy has proven to have several disadvantages. Most are rooted in the difficulty of acquiring the information necessary to set the price of each drug at just the right level – high enough to enable all essential participants in the distribution chain to earn a normal profit, but no higher. When regulators, relying on imperfect (or deliberately distorted) data, err on the low side, the result is a shortage of the drug at issue or an increase in low-quality drugs, either of which disadvantages potential consumers. When they err on the high side, the price ceiling ironically may function as a convenient target for the licensees or distributors (a phenomenon known as focal-point pricing), resulting in a retail price that is higher than it would be in an unregulated market.[111]

A more reliable way of curbing excessive prices is to structure a license in a way that harnesses competition. One technique has already been mentioned – ensuring that a sufficient number of licensees are operating in each country included in the territory such that the competition drives the prices down, even as every licensee is able to earn a reasonable profit.

Another less obvious technique is for the licensor to maintain a presence in the market by continuing to offer a branded version of the drug at issue. By setting the price of the branded version in poor countries at a no-profit level (much lower than the price in wealthier countries), the licensor can create a *de facto* ceiling price for the generics; no licensee will set the price of its products at a higher level, because customers will prefer the branded version. The licensor, unlike government regulators, can adjust the cap easily as production costs shift.

This approach helped Gilead considerably in driving down the prices of generic ARVs and HCV medicines in LMICs, particularly in countries where only one or two generics were competing. By contrast, the absence of a branded version of Delamanid (a powerful drug for drug-resistant tuberculosis) in South Africa enabled Mylan, the exclusive licensee, to charge high prices (US$640 for a six-month course of treatment), thereby sharply limiting access to the drug.[112]

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[110] See WHO, "Guideline on Country Pharmaceutical Pricing Policies," (2015).

[111] For documentation of these disadvantages of pharmaceutical price regulation, see Iain M Cockburn, Jean O Lanjouw, and Mark Schankerman, "Patents and the Global Dffusion of New Drugs," *American Economic Review* 106, no. 1 (2016); Emma Boswell Dean, "Who Benefits from Pharmaceutical Price Controls? Evidence from India," (Center for Global Development, 2019). For an eye-opening demonstration of the hazard of focal-point pricing provoked by pharmaceutical price regulation, see Jun Li and Di Wu, "The Price Effect of Drug Price Ceilings: Intended and Unintended Consequences," (2021). The latter relies upon a data set fortuitously generated by China's sudden abandonment of drug price regulation to confirm the danger originally highlighted by Thomas Schelling, *The Strategy of Conflict* (1960).

[112] See MSF, "DR-TB Drugs Under the Microscope" (6th ed. 2019), p. 6, available at https://endtb.org/sites/default/files/2019-11/MSF_Brief_DR-TB_Drugs_UTM_2019.pdf.

6. Regulatory Approval

Neither the branded version of a drug nor the generic versions authorized by an associated voluntary license can be marketed in a country without the approval of either the relevant NMRA or a regional regulatory authority. The following measures work well in minimizing the delays that are often associated with the regulatory processes in LMICs, particularly if pursued in combination: [113]

(1) As soon as possible after receiving approval from the FDA, EMA or other SRA, the licensor applies for marketing approval for the branded version of the drug in all of the countries that the VL will cover.
(2) The licensor waives its data-exclusivity rights with respect to the licensees – i.e., authorizes the licensees to use the data from the clinical trials for the branded version when seeking marketing approval for their generics.
(3) When appropriate, the licensor provides copies of approved drugs.
(4) The relevant NMRAs in the countries agree to process the applications for the branded version at least as quickly as the application for the generic versions.

The principal function of the fourth measure is to enable the licensor to employ the price-containment strategy discussed in the previous section – namely, using a low price for the branded version to create a ceiling for the generics. It might seem obvious that the NMRAs would not take longer to process applications for the branded version than applications for the generics, but experience has proved otherwise. Accordingly, making the partial waiver of data-exclusivity rights (item #2) conditional upon an explicit commitment not to "slow walk" the application for the branded version seems prudent.

If the licensor actively engages a national government in conjunction with the deployment of the license, then more complex, mutually beneficial deals may be feasible. For example, the licensor might agree to increase the percentage of licensees that consist of local producers (which, as we have seen, the nation's leaders typically strongly favor) if the relevant NMRA agrees to fast track the applications for marketing approval for both the branded version and the generic versions. Other ways of incentivizing the acceleration of the regulatory approval process may well emerge in the negotiation.

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[113] For documentation of the power of these measures, see Live Storehagen Dansie, Walter Denis Odoch, and Christine Årdal, "Industrial Perceptions of Medicines Regulatory Harmonization in the East African Community," *PLoS ONE* 14, no. 6 (2019); Abigail A. Ekeigwe, "Drug Manufacturing and Access to Medicines: The West African Story," *AAPS Open Access* 5, no. 3 (2019), https://link.springer.com/article/10.1186/s41120-019-0032-x; Stefanie Haas, "The Who Collaborative Registration Procedure for Medicines in Developing Countries" (Rheinischen Friedrich-Wilhelms-Universität Bonn, 2015); Bakani Mark Ncube, Admire Dube, and Kim Ward, "Establishment of the African Medicines Agency: Progress, Challenges and Regulatory Readiness," *Journal of Pharmaceutical Policy and Practice* 14 (2021); Margareth Ndomondo-Sigonda et al., "Medicines Regulation in Africa: Current State and Opportunities," *Pharm Med* 31 (2017).

A potential objection to this last suggestion is that NMRAs typically are legally autonomous (for good reason) and thus that other officials in the governments cannot simply direct them to accelerate evaluation of a particular drug. However, in our experience, the walls between governmental departments in poor countries are not watertight, and officials in each one often appropriately take into account suggestions and requests from officials in others.

7. Local Production

For the reasons explained above, in the future a licensor genuinely interested in maximizing public access to its products must include among the licensees one or more manufacturers based in the country to which the license will apply.

A possible objection to this recommendation: As noted above, the skeptics of local production have long contended that reliance on manufacturers located in poor countries will exacerbate the already serious problem of SFMPs. That might be true, but if so, the right response is to strengthen the systems of quality control and post-market surveillance discussed above, not to exclude local producers categorically. Many pharmaceutical manufacturers in poor countries have proved themselves to be capable of making and marketing the most sophisticated products.

Moreover, in one respect local production is likely to reduce rather than contribute to the incidence of SFMPs. As we have noted, one of the causes of the presence in poor-country markets of bad drugs is stockouts, which prompt dispensers to turn to illicit sources in order to address their customers' demands. Drug supplies derived from local manufacturers can be delivered more rapidly to dispensers than imports and do not languish in the limbo of customs. Thus their presence in the markets should reduce the frequency or shorten the duration of stockouts, which in turn should cause fewer SFMPs to enter the distribution chains.

8. Transparency

Pharmaceutical firms are often reluctant to make public the terms of the contracts through which they market their products in upper-income countries. Among the reasons for the reluctance are the disadvantages of exposing the presence of rebates and the unpopularity of some of the pricing strategies.

None of these considerations is relevant to the kind of licenses with which we are concerned. By contrast, publicizing the terms of a voluntary license has a major social-welfare benefit: it encourages other pharmaceutical firms to adopt similar strategies. It is thus not surprising that the leaders of the MPP, who have such long-term public interests in mind, strongly advocate transparency – and consistently publish the contracts that they negotiate. There is no good reason why bilateral voluntary licenses should not also be made public.

9. Intellectual Property

Should a VL be conditioned upon the availability in the relevant jurisdiction of intellectual-property protection for the drug in question? When addressing this controversial question, it is important to differentiate three types of IP shields that might be employed. The first and most familiar is patent protection. Less well known is data-exclusivity protection. The third is the protection that trademark law can provide to the names, symbols, packaging, and pill color selected by the licensor or licensees.[114]

On balance, it is undesirable for several reasons for a pharmaceutical firm to insist on patent protection for a particular drug in a particular jurisdiction as a prerequisite for issuing a voluntary. First, patent protection is not available for any pharmaceutical product in most least-developed countries or in most of the countries that are not (yet) members of the World Trade Organization. Thus, insisting on patent protection would exclude from the coverage of a license many of the countries most in need of access. Next, obtaining patent protection is time consuming, so making patent protection a precondition of a VL would likely delay access to the drugs at issue. Finally, the abusive ways in which some pharmaceutical firms have in the past deployed patents have made the leaders of many poor countries suspicious of them.

In the countries where it is available, data-exclusivity protection is more compatible with a voluntary license. As subsection 6, above, suggested, the licensor's ability to waive its data-exclusivity rights with respect to the licensees – but not for other generic manufacturers – can effectively protect the licensees against unauthorized competitors.

Trademark protection is potentially even more useful. The processes for reviewing trademark applications are faster (and far less expensive) than the processes associated with patent applications. Trademark law is less laden with unsavory history than patent law. Finally, sensibly designed trademarks and trade dress provide consumers useful information in differentiating authorized from unauthorized products.[115]

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[114] See, e.g., Ross Whitney Corp v. SKF, 207 F.2d 190 (9th Cir. 1953); Arul George Scaria and kavya mammen, "Non-Traditional Trademarks in the Pharmaceutical Sector: Non-Traditional Barriers to Access to Medicine?," in *The Protection of Non-Traditional Marks: Critical Perspectives*, ed. Irene Calboli and M.R.F. Senftleben (Oxford University Press, 2018).

[115] Filing trademark applications in multiple countries is also facilitated by the Madrid Protocol. Unfortunately, many developing countries are not yet members of the Protocol. (A map showing the current membership is set forth below.) The potential benefit of membership in facilitating VLs is one among several considerations that should prompt more LMICs to consider membership.

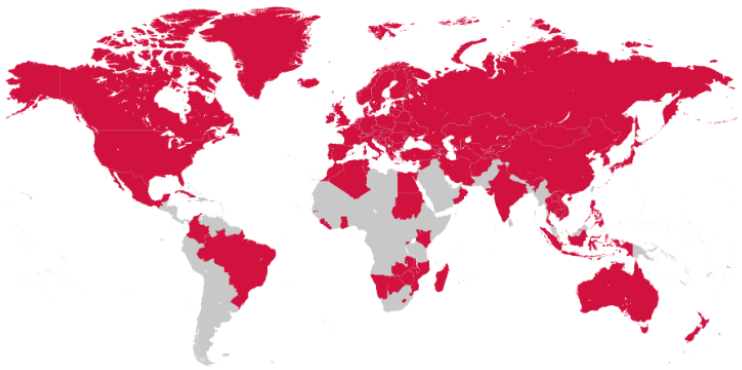
Against this backdrop, a licensor should apply for trademark protection as early as possible in every jurisdiction in the projected field of use. That would enable the licensor subsequently to shield its branded version against imitators. In addition, the licensor should consider developing a different label and pill color to designate licensed generics.[116] Diligent enforcement of those rights would then enable the licensor and licensees to suppress any confusingly similar unauthorized generics. That would both protect the licensees' market shares and shield the reputations of licensor and licensees.

To be sure, trademark protection would not prevent entry into the market of an unauthorized generic that does not suggest to consumers that it has received the endorsement of the innovator. But, in combination, the presence in the market of reasonably priced licensed generics, the barrier created by data exclusivity, and the reputational disadvantage of lack of endorsement by the innovator should keep such intrusions to a manageable minimum.

10. Capacity Building

One factor that unfortunately limits opportunities for voluntary licenses covering complex molecules is the lack of technical capacity on the part of potential licensees. In the past, this factor may have contributed to the absence of licenses granted by the developers of the mRNA-based COVID vaccines. In the future, it may impede issuance of licenses on monoclonal antibodies.

Concerns about technical capacity are amplified by the premium now being placed on the inclusion of local producers in the set of licensees. Generally speaking, the percentage of pharmaceutical firms in low-income and lower-middle-income countries that



Source: "Brazil Accedes to the Madrid Protocol: An Inside Story – and What Happens Next?" World Trademark Review (2019), https://www.lexology.com/library/detail.aspx?g=e52b5226-209e-496e-a78d-bd97235e348f.

[116] When selecting a shape or color, the Licensor should be careful to avoid a configuration that a court might subsequently deem to be "functional" and thus unprotectable. The more arbitrary, the better.

already have the skill necessary to produce – reliably and at scale – the most complex molecules is lower than that in upper-income countries.

Two strategies could be used to overcome this barrier. First, the intermediaries could assist potential licensees to acquire the necessary skills. An important venture of this sort is already underway. When the developers of the mRNA vaccines insisted that potential manufacturers in poor countries lacked the ability to produce generic versions of their products, the MPP and the WHO, with the financial support of several national governments, created a program to provide those manufacturers the necessary training.[117] Called the "mRNA Technology Transfer Programme," it aspires to share technical expertise concerning mRNA-based pharmaceutical products among both public and private institutions in low and middle-income countries.

Like many global-health initiatives, the Programme morphed during its emergence. Its designers expected – or hoped – to persuade Moderna or one of the other innovator firms to provide the Programme's participants access to the most recent technology in the field. Rebuffed, they instead created channels through which participants in the venture could exchange among themselves their rapidly developing expertise. Its current structure consists of a hub and spokes:

> The programme operates via a global collaborative network, comprising two core elements. The first is the South African Consortium, which includes Afrigen Biologics, Biovac and the South African Medical Research Council (SAMRC), collectively known as the 'Hub'. This consortium is responsible for the technology platform and product development. The second element consists of 14 further manufacturing partners located in different parts of the world.[118]

The Programme is not free of friction. Many of the participants are for-profit companies. As one might expect, some of their executives and investors have sought, when sharing expertise, to earn revenue or to secure other commercial advantages. This has prompted some critics to lament the Programme's failure to transform the fundamentally profit-driven structure of pharmaceutical innovation.[119]

Those criticisms are powerful, but should not obscure the substantial progress that the Programme has already made in enhancing the technical capacity of its participants. "From zero mRNA manufacturing capabilities in LMICS at the launch, the initiative

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[117] The complex set of discussions that gave rise to this program are summarized in Matthew Herder, Ximena Benavides, and Roojin Habibi, "'Our Project, Your Problem?' A Case Study of the Who's Mrna Technology Transfer Programme in South Africa," *PLOS global public health* 4, no. 9 (2024): 5-12.

[118] MPP, "Annual Report 2023," 54. The "partners" are located in Argentina, Bangladesh, Brazil, Egypt, India, Indonesia, Kenya, Nigeria, Pakistan, Senegal, Serbia, Tunisia, Ukraine and Vietnam.

[119] See Devika Dutt, Mariana Mazzucato, and Els Torreele, "An Mrna Technology Transfer Programme and Economic Sustainability in Health Care," *Bulletin of the World Health Organization* 102, no. 5 (2024); Herder, Benavides, and Habibi, "Case Study of the Mrna Technology Transfer Programme."

expects 11 state-of-the-art good manufacturing practices (GMP) certified mRNA manufacturing facilities to be launched in 10 countries by 2030 – two within the next year."[120] For present purposes, the most important effect of this upgrade is that, when the next pandemic occurs, many firms in poor countries will be better positioned to participate actively in the development and deployment of the vaccines and therapeutics we will need to fight it. At a minimum, they will be more capable of assuming the role of licensees. More optimistically, they will be better positioned to develop and test the necessary drugs themselves.

This accomplishment, however, is precarious. Unless these skills are put to use, they will atrophy or become outdated. The best way of preventing that would be for the leaders of the nations who stand to benefit from an increase in local production to agree to purchase products from the newly empowered manufacturers, even if they have to pay a premium for them. This theme was emphasized by the participants in a recent conference celebrating the progress already made by the Programme.[121] Outside of Brazil, it remains unclear whether that call will be heeded.

The second strategy for building capacity would require a collaboration between the set of potential licensors and the governments of the countries in which are located potential licensees. The following brief detour will help illuminate its shape and potential.[122]

In early modern Europe, the apprenticeship system emerged as a highly effective mechanism for transmitting technical knowledge. During this period, if you wanted to learn a skilled trade (e.g., baking or metalworking), you did not go to school or read a book; you became an apprentice to a master in that trade. The form of such apprenticeships varied significantly by region, but the most successful and influential variant was the model formalized (partly by law, partly by custom) in London and then mimicked in many other English cities. In brief, an apprentice worked for a minimum of seven years, the end of which had to be after the apprentice turned 24 years old. The master provided the apprentice training, food, and housing – but usually not wages. The apprentice, in turn, provided labor – which, over the course of the apprenticeship, gradually became increasingly skilled. Masters were required to register apprenticeship indentures (i.e., contracts) with city authorities. An apprentice who completed his term of service frequently set up shop on his own (and became a freeman of the city) and eventually took on apprentices of his own. This system was widely used. In the sixteenth and seventeenth centuries, roughly 10% of

[120] Kerry Cullinan, "Sustainability Is the Focus of Who's Mrna Vaccine Programme as Partners Look Beyond Covid," *Health Policy Watch* (2024), https://perma.cc/QFJ7-TEBH.

[121] See ibid.

[122] The next five paragraphs are adapted from William Fisher, Ruth Okediji, and Padmashree Gehl Sampath, "Fostering Production of Pharmaceutical Products in Developing Countries," *Michigan Journal of International Law* 43 (2021)..

the population of London were apprentices, and two thirds of adult male residents of the city had at some point served as apprentices.[123]

Apprenticeship during this period had several social and economic functions, including the socialization of unruly adolescents, the maintenance of class hierarchies, and (in conjunction with the guild system) limiting the supply of skilled labor and thus sustaining the prices that skilled laborers could charge. Historians continue to debate the relative importance of these functions. But on one issue there is little disagreement: the apprenticeship model proved a highly effective mechanism for preserving and transmitting technical information. After the industrial revolution, apprenticeship was displaced in most fields by other forms of technical training (or by no training at all), but it survives (and indeed flourishes) today in some sectors of the economy – notably, medicine in the U.S. (through the residency system in "teaching hospitals"); private law practice (through the "associate" system in law firms – itself a vestige of the dominant system of legal education in the 18th and early 19th centuries); boatbuilding; and in many industries in Germany.[124]

This system could be adapted to strengthen the skills that employees of firms in poor countries would need to produce complex pharmaceutical products. Without impairing the volume or pace of production, the innovator firms that first developed those products could take on, as apprentices, scientists employed by existing or prospective pharmaceutical firms in developing countries. Working alongside the innovators' scientists, the apprentices would absorb crucial technical knowledge and then return to their own countries of residence to set up and run similar production facilities. They would be replaced by another cohort of apprentices, who would in turn return to their country of origin, and so forth. In this way, firms in developing countries would have access to the most current knowledge concerning how best to produce safe and efficacious drugs.

The feasibility of such a system is suggested by the fact that apprenticeships have long been employed to good effect in German chemical and pharmaceutical firms.[125] Increasingly, pharmaceutical firms in other countries, including the U.S., are relying on them to train skilled workers.[126] To be sure, the level at which the proposed program would

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[123] *See* Prak Maarten and Patrick Wallis, *Apprenticeship in Early Modern Europe* (Cambridge: Cambridge University Press, 2019); Patrick Wallis, "Apprenticeship and Training in Premodern England," *Journal of Economic History* 68 (2008).

[124] *See, e.g.*, Richard Heitmiller et al., "Apprenticeships: Preserving the Commitment in Surgical Education," *Journal of Surgical Education* 65 (4): 259-262; Stan Grayson, "The Little Engine that Could – 100 Years of Beetle Cats," *Wooden Boat* (September/October 2020); Lutz Raphael, "Knowledge, Skills, Craft? The Skilled Worker in West German Industry and the Resilience of Vocational Training, 1970–2000," *German History* 37, no. 3 (2019).; Dietmar Harhoff and Thomas J. Kane, "Is the German Apprenticeship System a Panacea for the U. S. Labor Market?," *Journal of Population Economics* 10 (1997): 174-75.

[125] A description of Bayer's apprenticeship program for "bioscientists" is available at https://karriere.bayer.de/sites/g/files/kmftyc1001/files/2019-05/EB_A4_Biowissenschaftler_180212_EN_Preview.pdf.

[126] *See, e.g.*, Association of the British Pharmaceutical Industry, "Apprenticeships Hit 4-year High in British Pharmaceutical Industry," Press Release, July 1, 2018; "Should Your Kids Become Process Apprentices," Process Engineering, March/April 2009: 5.

operate is different. Instead of training technicians, the goal would be to train the scientists and managers who would be responsible for establishing and overseeing new and complex manufacturing processes. But if apprenticeship can be employed to teach advanced surgical techniques,[127] it ought to work in teaching novel pharmaceutical manufacturing methods.

Creation of a system of this sort would require three things. First, systems for selecting, coordinating, and supporting the apprentices would have to be created by the governments of developing countries – in much the same way that apprenticeship was regulated by the City of London in the seventeenth century. Second, the firms in developing countries who benefitted from this model would have to commit credibly not to export drugs to developed countries – and the governments in those countries would have to back the firms' commitment. Last but not least, the innovator firms would have to be persuaded to participate genuinely in the system. That, in turn, would require the innovators to take a long-term view – to recognize the advantages, when the next pandemic arrives, of having already in place a network of skilled potential licensees in poor countries.

11. Scope

We come, finally, to the most serious of the impediments to more effective use of the strategy of voluntary licensing. As we have seen, the licensor determines the set of countries in which the licensees may distribute their generic products. The sets that have been selected by different firms have been, to some degree, idiosyncratic. However, in the 20 years since Gilead first pioneered this approach, there has been one overall trend: the sets have gotten smaller. Roughly speaking, the constriction has occurred at the top of the income scale. While all licenses have continued to include the poorest countries, the most recent licenses have excluded many upper-middle-income countries, in which reside many poor people vulnerable to the disease at which the relevant drugs are aimed. If this trend continues, voluntary licensing will gradually lose its potential for alleviating the global health crisis.

Reversing the trend will not be easy, because currently none of the constituencies whose collaboration underlies deals of this sort have strong interests in expanding their geographic reach. The licensors certainly do not. The principal cause of the trend is their belief that their profits will be larger if they sell branded versions of their products in middle-income countries than if they license other firms to sell generic versions there. To be sure, the licensees are disadvantaged by the narrowing, because it reduces the size of their markets. However, if the licensor is careful to adjust the number of licensees so as not to overcrowd the field, that disadvantage disappears. The leaders of the nations that are included in the shrunken deals have no reason to object, while the leaders of the nations

[127] *See* Elizabeth H. Stephens and Joseph A. Dearani, "On Becoming a Master Surgeon: Role Models, Mentorship, Coaching, and Apprenticeship," *Annals of Thorasic Surgery* (Pre-proof) (2020): 8; William Nolan, *The Making of a Surgeon* (1970).; Bennet A. Butler, Cameron M. Butler, and Terrance D. Peabody, "Cognitive Apprenticeship in Orthopaedic Surgery: Updating a Classic Educational Model," *Journal of Surgical Education* 76, no. 4 (2019).

that are excluded have no voice. Typically, the only party that advocates broad coverage is the MPP. In the subset of cases in which licenses are conducted through it, the MPP negotiators do seem to favor generosity. However, their power in this regard is limited. If they press too firmly, the licensor can always bypass them and issue bilateral licenses. In short, no one in the inner circle currently has both incentive and ability to insist on a large footprint.

There appears to be only two ways in which this unfortunate trend might be reversed. Either we must persuade the licensors that they could preserve their profits without narrowing the licenses' scope, or we must find a way to alter the incentives of one or more of the critical parties.

An example of the first approach would be to encourage the firms, when shaping their voluntary licenses, to make greater use of the differential-pricing principle discussed in the preceding chapter. The flat royalties that appear in most voluntary licenses are not set in stone. If the firms increased the royalties that the licensees pay when distributing products in upper-middle-income countries, they could approximate the revenues they currently earn by selling branded versions of their drugs in those markets. From the standpoint of global social welfare, the advantage of persuading them to make this adjustment is that, typically, the production costs of the generic versions authorized by voluntary licensing are substantially lower than the production costs associated with the branded versions. (Witness, for example, the dramatic decline in the price of Sovaldi in Egypt when Gilead's branded products, ostensibly sold at "no profit," were displaced by locally produced generic versions.) Thus, the prices paid by the residents (or public-health services) of the middle-income countries would be significantly lower.

Some of the firms using voluntary licensing have already begun to implement mild versions of this strategy. The most recent deals involving COVID therapeutics include higher royalties for products distributed in middle-income countries, particularly when the distribution channel is commercial rather than public. Perhaps the firms can be persuaded that, by using more sharply "tiered" royalties, they could include more countries in their licenses without sacrificing revenue.

This strategy is worth trying, but frankly we doubt that it will work. The licensors' negotiators are not obtuse. Most likely, they are well aware of the option of using tiered royalties – and have decided not to go that route. Finding some way to change their incentives seems a better bet.

A few levers that might be employed for this purpose lurk in the narratives with which we began. Recall that one of the grounds on which Gilead was criticized for the narrowness of its recent lenacapavir license is that it failed to include some of the countries in which clinical trials for that very drug had been conducted. This suggests that, in the future, the governments of upper-middle-income countries might use to their advantage the interests of the firms in testing drugs on their populations – by conditioning permission to conduct clinical trials within their borders on commitments to include their countries in any voluntary licenses subsequently granted on the drugs in question.

In theory, a bank shot by the government of a high-income country is also imaginable. Suppose, for example, that one of the larger European countries altered its reference pricing system to include in the basket all of the upper-middle-income countries with which we are presently concerned. That would put pressure on the firms to extend voluntary licenses to those countries (perhaps using tiered royalties of the sort described above), rather than sell branded versions at medium prices in those countries.

These potential maneuvers are intriguing, but neither is likely to exert significant pressure on the firms. More promising would be conditions imposed on the grants or licenses upon which their primary businesses depend. Options of those sorts will be discussed in Chapters 9 and 10.

References

Abbott, Frederick, and Jerome H. Reichman. "The Doha Round's Public Health Legacy: Strategies for the Production and Diffusion of Patented Medicines under the Amended Trips Provisions." *Journal of International Economic Law* 10, no. 4 (2007): 921-87.

Abosheaishaa, Hazem, Abdelmalek Abdelghany, Omar Abdelhalim, Islam Mohamed, Samah Morsi, Mohammed Youssef, Ahmed Salem*, et al.* "The Egyptian Journey from Having the Highest Prevalence of Hepatitis C Virus to Being the First to Achieve "Gold Tier" in Conquering the Disease." *Proceedings - Baylor University. Medical Center* 37, no. 5 (2024): 877-83.

Aizenman, Nurith. "Moderna Won't Share Its Vaccine Recipe. Who Has Hired an African Startup to Crack It." *Nationa Public Radio* (2021). Published electronically October 19, 2021. https://www.npr.org/sections/goatsandsoda/2021/10/19/1047411856/the-great-vaccine-bake-off-has-begun.

al., American Federation of Teachers et. "Please Extend the Wto Trips Decision to Treatments and Tests and Support Countries Using Wto Flexibilities to Access Covid-19-Related Medical Technologies." (Augusr 23, 2022 2022).

Anderson, Anne-Marie, and Richard Kish. "Rewarding Performance through Sustainability-Linked Bonds." *Economic affairs (Harlow)* 44, no. 2 (2024): 294-319.

Andrieux-Meyer, Isabelle, Jennifer Cohn, Evaldo S. Affonso de Araújo, and Saeed S. Hamid. "Disparity in Market Prices for Hepatitis C Virus Direct-Acting Drugs." *The Lancet global health* 3, no. 11 (2015): e676-e77.

Associations, European Federation of Pharmaceutical Industries and. "A Fact-Based Analysis of the Trips Waiver Extension." (September 30, 2022 2022).

Baker, Brook K. "A Sliver of Hope: Analyzing Voluntary Licenses to Accelerate Affordable Access to Medicines." *Northeastern University Law Review* 10, no. 2 (2018): 226-315.

Bank, World. "Transforming Egypt's Healthcare System Project." 2018.

Barber, Melissa J., Dzintars Gotham, Giten Khwairakpam, and Andrew Hill. "Price of a Hepatitis C Cure: Cost of Production and Current Prices for Direct-Acting Antivirals in 50 Countries." *Journal of Virus Eradication* 6, no. 3 (2020): 100001-01.

Bate, Roger. "Local Pharmaceutical Production in Developing Countries: How Economic Protectionism Undermines Access to Quality Medicines." (2008).

Benzaken, Adele S., Gerson F.M. Pereira, and Lendel Costa. "Antiretroviral Treatment, Government Policy and Economy of Hiv/Aids in Brazil: Is It Time for Hiv Cure in the Country?". *AIDS Research and Therapy* 16, no. 19 (2019).

Board, Editorial. "The World Needs Many More Coronavirus Vaccines." *New York Times*, April 24, 2021.

Burrows, Robert, and Ellen Lambrix. "Mrna Vaccines: A Growing and Complex Ip Landscape." *Vaccine Insights* 1, no. 4 (2022): 191-99.

Butler, Bennet A., Cameron M. Butler, and Terrance D. Peabody. "Cognitive Apprenticeship in Orthopaedic Surgery: Updating a Classic Educational Model." *Journal of Surgical Education* 76, no. 4 (2019): 931-35.

Ciza, P.H., P.-Y.Sacre, C.Waffo, L.Coïc, J.K.Mbinzeb H.Avohoua, R.Ngonoc,, and PhHuberta R.D. Marinia, E.Ziemonsa. "Comparing the Qualitative Performances of Handheld Nir and Raman Spectrophotometers for the Detection of Falsified Pharmaceutical Products." *Talanta* 202 (2019): 469-78.

Coalition, Hep C. "Sofosbuvir Turns 5 Years Old: The Vast Majority of People with Chronic Hepatitis C Still Have Not Been Treated." 2018.

Cockburn, Iain M, Jean O Lanjouw, and Mark Schankerman. "Patents and the Global Dffusion of New Drugs." *American Economic Review* 106, no. 1 (2016): 136-64.

"Collaboration Agreement between Pfizer, Inc. And Biontech Se." 2020.

Commission, US International Trade. "Covid-19 Diagnostics and Therapeutics: Supply, Demand, and Trips Agreement Flexibilities." 2023.

Corbett, Kizzmekia S., Darin K. Edwards, Sarah R. Leist, Olubukola M. Abiona, Seyhan Boyoglu-Barnum, Rebecca A. Gillespie, Sunny Himansu*, et al.* "Sars-Cov-2 Mrna Vaccine Design Enabled by Prototype Pathogen Preparedness." *Nature (London)* 586, no. 7830 (2020): 567-71.

Correa, Carlos. "Expanding the Production of Covid-19 Vaccines to Reach Developing Countries: Lift the Barriers to Fight the Pandemic in the Global South." South Centre, 2021.

Cullinan, Kerry. "Sustainability Is the Focus of Who's Mrna Vaccine Programme as Partners Look Beyond Covid." *Health Policy Watch* (2024). Published electronically November 20, 2024. https://perma.cc/QFJ7-TEBH.

Dansie, Live Storehagen, Walter Denis Odoch, and Christine Årdal. "Industrial Perceptions of Medicines Regulatory Harmonization in the East African Community." *PLoS ONE* 14, no. 6 (2019).

de Mariz, Frederic, Pieter Bosmans, Daniel Leal, and Saumya Bisaria. "Reforming Sustainability-Linked Bonds by Strengthening Investor Trust." *Journal of risk and financial management* 17, no. 7 (2024): 290.

Dean, Emma Boswell. "Who Benefits from Pharmaceutical Price Controls? Evidence from India." Center for Global Development, 2019.

Dutt, Devika, Mariana Mazzucato, and Els Torreele. "An Mrna Technology Transfer Programme and Economic Sustainability in Health Care." *Bulletin of the World Health Organization* 102, no. 5 (2024): 344-51.

Dyer, Owen. "Gilead to License Generic Lenacapavir for Hiv Prophylaxis in 120 Lower Income Countries." *BMJ (Online)* 387 (2024): q2200.

Ekeigwe, Abigail A. "Drug Manufacturing and Access to Medicines: The West African Story." *AAPS Open Access* 5, no. 3 (2019). https://link.springer.com/article/10.1186/s41120-019-0032-x.

Elizabeth H. Stephens, and Joseph A. Dearani. "On Becoming a Master Surgeon: Role Models, Mentorship, Coaching, and Apprenticeship." *Annals of Thorasic Surgery* (Pre-proof) (2020).

Figueroa, J. Peter, Maria Elena Bottazzi, Peter Hotez, Carolina Batista, Onder Ergonul, Sarah Gilbert, Mayda Gursel*, et al.* "Urgent Needs of Low-Income and Middle-Income Countries for Covid-19 Vaccines and Therapeutics." *The Lancet (British edition)* 397, no. 10274 (2021): 562-64.

Fiocruz. "Technological Order Agreement Entered into by Fundacao Oswaldo Cruz — Fiocruz, Instituto De Tecnologia Em Imunobiologicos — Bio-Manguinhos and Astrazeneca Uk, Ltd.", 2020.

Fisher, William, Ruth Okediji, and Padmashree Gehl Sampath. "Fostering Production of Pharmaceutical Products in Developing Countries." *Michigan Journal of International Law* 43 (2021).

Fisher, William, and Cyrill P. Rigamonti. "The South Africa Aids Controversy: A Case Study in Patent Law and Policy." *Harvard Law School Case Study* (2005). https://ipxcourses.org/GPP/South_Africa_AIDS_Controversy.pdf.

Forum, World Economic. "The Art and Science of Eliminating Hepatitis: Egypt's Experience." 2022.

———. "What Are Sustainability Linked Bonds and How Can They Support the Net-Zero Transition?", 2022.

Frank, Christina, Mostafa K. Mohamed, G. Thomas Strickland, Daniel Lavanchy, Ray R. Arthur, Laurence S. Magder, Taha El Khoby*, et al.* "The Role of Parenteral Antischistosomal Therapy in the Spread of Hepatitis C Virus in Egypt." *The Lancet* 355, no. 9207 (2000): 887-91.

Gaviria, Mario, and Burcu Kilic. "A Network Analysis of Covid-19 Mrna Vaccine Patents." *Nature biotechnology* 39, no. 5 (2021): 546-48.

Gilead. "Gilead Signs Royalty-Free Voluntary Licensing Agreements with Six Generic Manufacturers to Increase Access to Lenacapavir for Hiv Prevention in High-Incidence, Resource-Limited Countries." news release, 2024, https://perma.cc/4U9L-NSAW.

Gore, Charles, Sébastien Morin, John-Arne Røttingen, and Marie Paule Kieny. "Negotiating Public-Health Intellectual Property Licensing Agreements to Increase Access to Health Technologies: An Insider's Story." *BMJ global health* 8, no. 9 (2023): e012964.

Gower, Erin, Chris Estes, Sarah Blach, Kathryn Razavi-Shearer, and Homie Razavi. "Global Epidemiology and Genotype Distribution of the Hepatitis C Virus Infection." *Journal of hepatology* 61, no. 1 (2014): S45-S57.

Guasco, Rick. "Gilead Licenses Generic Version of Lenacapavir as Prep in 120 Countries Outside the U.S." *Positively Aware* (2024). Published electronically October 2, 2024. https://perma.cc/EH72-EY99.

Haas, Stefanie. "The Who Collaborative Registration Procedure for Medicines in Developing Countries." Rheinischen Friedrich-Wilhelms-Universität Bonn, 2015.

Harhoff, Dietmar, and Thomas J. Kane. "Is the German Apprenticeship System a Panacea for the U. S. Labor Market?". *Journal of Population Economics* 10 (1997): 171-96.

Hassanin, Ahmed, Serageldin Kamel, Iman Waked, and Meredith Fort. "Egypt's Ambitious Strategy to Eliminate Hepatitis C Virus: A Case Study." *Global health science and practice* 9, no. 1 (2021): 187-200.

Herder, Matthew, Ximena Benavides, and Roojin Habibi. "'Our Project, Your Problem?' A Case Study of the Who's Mrna Technology Transfer Programme in South Africa." *PLOS global public health* 4, no. 9 (2024): e0003173.

Higgins-Dunn, Noah. "Moderna Ceo Says He's Not Losing Any Sleep over Biden's Support for Covid-19 Vaccine Waiver." *Fierce Pharma* (2021). Published electronically May 6, 2021. https://www.fiercepharma.com/pharma/moderna-ceo-says-he-s-not-losing-any-sleep-over-biden-s-endorsement-for-covid-19-ip-waiver.

International, Knowledge Ecology. "Kei Asks Ftc to Investigate Gilead Effort to Control Market for Aids Drugs Ingredients." news release, February 15, 2007, https://perma.cc/N4Q3-X3SA.

Iyengar, Swathi, Kiu Tay-Teo, Sabine Vogler, Peter Beyer, Stefan Wiktor, Kees de Joncheere, Suzanne Hill, and Sanjay Basu. "Prices, Costs, and Affordability of New Medicines for Hepatitis C in 30 Countries: An Economic Analysis." *PLOS Medicine* 13, no. 5 (2016): e1-e1002032.

Kamal-Yanni, Mohga. "Hepatitis C Drug Affordability." *The Lancet global health* 3, no. 2 (2015): e73-e74.

Kaplan, Warren, and Richard Laing. "Local Production of Pharmaceuticals: Industrial Policy and Access to Medicines." *HNO Discussion Paper 32036* (2005).

Kovacs, Stephanie, Stephen E. Hawes, Stephen N. Maley, Ling Wong2 Emily Mosites1, and 3 Andy Stergachis1, 4. "Technologies for Detecting Falsified and Substandard Drugs in Low and Middle-Income Countries." *PLoS ONE* 9, no. 3 (2014).

Levi, Jacob, Alice Raymond, Anton Pozniak, Pietro Vernazza, Philipp Kohler, and Andrew Hill. "Can the Unaids 90-90-90 Target Be Achieved? A Systematic Analysis of National Hiv Treatment Cascades." *BMJ global health* 1, no. 2 (2016): e000010-e10.

Li, Jun, and Di Wu. "The Price Effect of Drug Price Ceilings: Intended and Unintended Consequences." 2021.

Liu, Chenglin. "Beyond Compulsory Licensing: Pfizer Shares Its Covid-19 Medicines with the Patent Pool." *Legislation and Public Policy* 25 (2021).

Loftus, Peter. "Pfizer, Moderna and J&J Face Shareholder Pressure to Broaden Covid-19 Vaccine Access." *Wall Street Journal*, March 22, 2022 2022.

Looney, William. "The Medicines Patent Pool Plots a Post-Pandemic Future: Interview with Director Charles Gore." *In Vivo*, September 20, 2021.

Luangasanatip, Nantasit, Panarasri Khonputsa, Ce´line Caillet, 3 Serena Vickers2, 4,, and Facundo M. Ferna´ndez5 Stephen Zambrzycki5, Paul N. Newton2,3,4, Yoel Lubell1,3. "Implementation of Field Detection Devices for Antimalarial Quality Screening in Lao Pdr—a Cost-Effectiveness Analysis." *PLOS Neglected Tropical Diseases* 15, no. 9 (2021).

Lyu, Mengru, Jiyuan Chen, Yeheng Peng, Fang Han, Luyao Gong, Jingfei Guo, Lijuan Tian, and Yuan Gao. "The Global Patent Landscape of Mrna for Diagnosis and Therapy." *Nature biotechnology* 41, no. 9 (2023): 1193-99.

Maarten, Prak, and Patrick Wallis. *Apprenticeship in Early Modern Europe.* Cambridge: Cambridge University Press, 2019.

Marshall, Alison D., Evan B. Cunningham, Stine Nielsen, Alessio Aghemo, Hannu Alho, Markus Backmund, Philip Bruggmann*, et al.* "Restrictions for Reimbursement of Interferon-Free Direct-Acting Antiviral Drugs for Hcv Infection in Europe." *THE LANCET GASTROENTEROLOGY AND HEPATOLOGY* 3, no. 2 (2018): 125-33.

Moderna. "Statement by Moderna on Intellectual Property Matters during the Covid-19 Pandemic." news release, October 8, 2020, 2020, https://perma.cc/R9VB-2ULH.

Moore, Sam, Edward M. Hill, Louise Dyson, Michael J. Tildesley, and Matt J. Keeling. "Retrospectively Modeling the Effects of Increased Global Vaccine Sharing on the Covid-19 Pandemic." *Nature Medicine* 28 (2022): 2416–23.

MPP. "Accelerating Access through Community Partnership: Annual Report 2023." 2024.

———. "Voluntary Licensing: Right for Health, Smart for Business." 2024.

MSF. "Not Even Close." (2017).

Ncube, Bakani Mark, Admire Dube, and Kim Ward. "Establishment of the African Medicines Agency: Progress, Challenges and Regulatory Readiness." *Journal of Pharmaceutical Policy and Practice* 14 (2021).

Ndomondo-Sigonda, Margareth, Jacqueline Miot, Shan Naidoo, Alexander Dodoo4, and Eliangiringa Kaale5. "Medicines Regulation in Africa: Current State and Opportunities." *Pharm Med* 31 (2017): 383-97.

Neroulias, Nicole. "Activists: Deny Patent to Gilead." *East Bay Times*, May 11, 2006 2006.

Nolan, William. *The Making of a Surgeon.* 1970.

Organization, World Trade. "Communication from India and South Africa: Waiver from Certain Provisions of the Trips Agreement for the Prevention, Containment and Treatment of Covid-19." 2020.

———. "Communication from the African Group, the Plurinational State of Bolivia, Egypt, Eswatini, Fiji, India, Indonesia, Kenya, the Ldc Group, Maldives, Mozambique, Mongolia, Namibia, Pakistan, South Africa, Vanuatu, the Bolivarian Republic of Venezuela and Zimbabwe: Waiver from Certain Provisions of the Trips Agreement for the Prevention, Containment and Treatment of Covid-19." 2021.

———. "Communication from the European Union to the Council for Trips: Draft General Council Declaration on the Trips Agreement and Public Health in the Circumstances of a Pandemic." 2021.

———. "Council for Trips Paragraph 8 of the Ministerial Decision on the Trips Agreement: Informal Thematic Session for External Stakeholder Input, Report by the Chair." 2024.

———. "Ministerial Decision on the Trips Agreement." Ministerial Conference, Twelfth Session, 2022.

———. "Paragraph 8 of the Ministerial Decision on the Trips Agreement Adopted on 17 June 2022: Report to the General Council." 2024.

Ozawa, Sachiko, Daniel R. Evans, Sophia Bessias, and Deson G. Haynie. "Prevalence and Estimated Economic Burden of Substandard and Falsified Medicines in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis." *JAMA Network Open* 1, no. 4 (2018): e181662.

Petruzziello, Arnolfo, Samantha Marigliano, Giovanna Loquercio, Anna Cozzolino, and Carmela Cacciapuoti. "Global Epidemiology of Hepatitis C Virus Infection: An up-Date of the Distribution and Circulation of Hepatitis C Virus Genotypes." *World Journal of Gastroenterology* 22, no. 34 (2016): 7824-40.

Pfizer. "Pfizer and Biontech Announce Collaboration with Biovac to Manufacture and Distribute Covid-19 Vaccine Doses within Africa." news release, July 21, 2021, 2021, https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-announce-collaboration-biovac.

Pincombe, Morgan, and Javier Guzman. "Lessons from Expanding Access to Covid-19 Treatments in Lmics through Voluntary Licensing." Center for Global Development, 2022.

Policy, Global Commission for Post-Pandemic. "Covid-19 Vaccine Production, to January 31st 2022." 2022.

Pool, Medicines Patent. "Report to the Who Expert Committee on the Selection and Use of Essential Medicines." 2019.

Rahman, Fifa. "Malaysia Inclusion in Gilead Voluntary Licence – a Product of Compulsory Licence Pressure." *Health Policy Watch* (2017). Published electronically August 24, 2017. https://perma.cc/MGN7-938K.

Rangam, V. Kasturi. "Gilead: Hepatitis C Access Strategy (a)." Harvard Business School Case Study 9-515-025, 2023.

Rangan, V. Kasturi. "Gilead: Hepatitis C Access Strategy (B)." In *Harvard Business School Case Study 9-515-044*, 2016.

Raphael, Lutz. "Knowledge, Skills, Craft? The Skilled Worker in West German Industry and the Resilience of Vocational Training, 1970–2000." *German History* 37, no. 3 (2019): 359=73.

Representative, United States Trade. "Statement from Ambassador Katherine Tai on the Covid-19 Trips Waiver." news release, May 5, 2021, 2021, https://perma.cc/JN53-Y5UW.

Rong, Libin, and Alan S. Perelson. "Treatment of Hepatitis C Virus Infection with Interferon and Small Molecule Direct Antivirals: Viral Kinetics and Modeling." *Critical reviews in immunology* 30, no. 2 (2010): 131-48.

Sanger-Katz, Margot. "$1,000 Hepatitis Pill Shows Why Fixing Health Costs Is So Hard." *New York Times*, August 2, 2014 2014.

Scaria, Arul George, and kavya mammen. "Non-Traditional Trademarks in the Pharmaceutical Sector: Non-Traditional Barriers to Access to Medicine?". In *The Protection of Non-Traditional Marks: Critical Perspectives*, edited by Irene Calboli and M.R.F. Senftleben: Oxford University Press, 2018.

Schelling, Thomas. *The Strategy of Conflict.* 1960.

Schwambach, Karin Hepp, Mareni Rocha Farias, Giácomo Balbinotto Neto, and Carine Raquel Blatt. "Cost and Effectiveness of the Treatment of Chronic Hepatitis C in Brazil: Real-World Data." *Value in health regional issues* 23 (2020): 49-54.

Sciences, Gilead. "2017 Amended & Restated Voluntary Hcv License Agreement." (2017). https://www.gilead.com/-/media/files/pdfs/other/form-ar-hcv-license-agmt-gild-11202017.pdf?la=en&hash=EA13A53F28CE66946255B7369B57EEFE.

———. "Chronic Hepatitis C Treatment Expansion." news release, November 17, 2017, 2017, https://perma.cc/QEL6-NB7M.

———. "Chronic Hepatitis C Treatment Expansion." news release, October 20, 2014, 2014, https://perma.cc/S9V2-DKC9.

———. "Impact Report: Access Operations and Emerging Markets." 2017.

Sellevold, Diana, and Philip Larsen. "Sustainability-Linked Bonds an Examination of Yield Differences between Sustainability-Linked and Conventional Bonds." OsloMet-Storbyuniversitetet, 2023.

Shakeri, Ahmad, Narthaanan Srimurugathasan, Katie J. Suda, Tara Gomes, and Mina Tadrous. "Spending on Hepatitis C Antivirals in the United States and Canada, 2014 to 2018." *Value in health* 23, no. 9 (2020): 1137-41.

Shores, Dan, Dylan Haversack, and Andrew J. Storaska. "The Mrna Ip and Competitive Landscape through One Year of the Covid-19 Pandemic — Part I." *IP Watch* (2021). Published electronically April 11, 2021. https://ipwatchdog.com/2021/04/11/mrna-ip-competitive-landscape-one-year-covid-19-pandemic-part/id=132130/.

———. "The Mrna Ip and Competitive Landscape through One Year of the Covid-19 Pandemic — Part Ii." *IP Watch* (2021). Published electronically April 11, 2021. https://ipwatchdog.com/2021/04/21/mrna-ip-competitive-landscape-translate-bio-arcturus-etherna-startups-lnp-technology-part-ii/id=132287/.

———. "The Mrna Ip and Competitive Landscape through One Year of the Covid-19 Pandemic — Part Iii." *IP Watch* (2021). Published electronically April 11, 2021. https://ipwatchdog.com/2021/04/30/mrna-patent-competitive-landscape-pioneers-litigation-outlook-big-pharmas-next-moves-part-iii/id=132936/.

Storz, Ulrich. "The Covid-19 Vaccine Patent Race." *Nature biotechnology* 40, no. 7 (2022): 1001-04.

Thambisetty, Siva, Aisling McMahon, Luke McDonagh, Hyo Yoon Kang, and Graham Dutfield. "Addressing Vaccine Inequity during the Covid-19 Pandemic: The Trips Intellectual Property Waiver Proposal and Beyond." *Cambridge law journal* 81, no. 2 (2022): 384-416.

UNDP. "Global Dashboard for Vaccine Equity." 2024.

Velásquez, Germán. "The Use of Trips Flexibilities for the Access to Hepatitis C Treatment." South Centre, 2018.

Venkatesan, Priya. "New Licences for the Covid-19 Technology Access Pool." *The Lancet. Microbe* 4, no. 12 (2023): e971-e71.

Waked, Imam. "Case Study of Hepatitis C Virus Control in Egypt: Impact of Access Program." *Antiviral therapy* 27, no. 2 (2022): 13596535211067592-92.

Wallis, Patrick. "Apprenticeship and Training in Premodern England." *Journal of Economic History* 68 (2008): 832-61.

Wang, Wenbo, Matthew D. Keller, Ted Baughman, and Benjamin K. Wilson. "Evaluating Low-Cost Optical Spectrometers for the Detection of Simulated Substandard and Falsified Medicines." *Applied Spectroscopy* 74, no. 3 (2020): 323-33.

Wanis, Heba. "Egypt Will Not Patent New Hepatitis C Drug." (2014). Published electronically May 25, 2014. https://perma.cc/BSK5-NVMN.

WHO. "Accelerating Access to Hepatitis C Diagnostics and Treatment: Overcoming Barriers in Low and Middle-Income Countries." 2020.

———. "Egypt Becomes the First Country to Achieve Who Validation on the Path to Elimination of Hepatitis C." news release, October 9, 2023, 2023, https://perma.cc/KJZ9-J45S.

———. "Guideline on Country Pharmaceutical Pricing Policies." 2015.

———. "Hepatitis C." https://perma.cc/4AQZ-54JP.

———. "Patent Situation of Key Products for Treatment of Hepatitis C: Daclatasvir." 2016.

———. "Patent Situation of Key Products for Treatment of Hepatitis C: Ledipasvir." 2016.

———. "Patent Situation of Key Products for Treatment of Hepatitis C: Paritaprevir/Ombitasvir/Dasabuvir." 2016.

———. "Patent Situation of Key Products for Treatment of Hepatitis C: Simeprevir." 2016.

———. "Patent Situation of Key Products for Treatment of Hepatitis C: Sofosbuvir." 2016.

———. "A Study of the Public Health and Socioeconomic Impact of Substandard and Falsified Medical Products." 2017.

———. "Who Initiative Signs New Licensing Agreements on Covid-19 Technologies." news release, August 29, 2023, 2023, https://perma.cc/3477-5SQF.

"Who's Tedros Says Covid-19 Vaccine Inequity Creates 'Two-Track Pandemic'." *Reuters* (2021). Published electronically June 2, 2021. https://www.reuters.com/business/healthcare-pharmaceuticals/whos-tedros-says-covid-19-vaccine-inequity-creates-two-track-pandemic-2021-06-07/.

Yabré, Moussa, Abdoul Karim Sakira, Moumouni Band´e, Bertrand W.F. Goumbri, Sandrine M. Ouattara, Souleymane Fofana, and Touridomon Issa Som´e. "Detection of Falsified Antimalarial Sulfadoxine-Pyrimethamine and Dihydroartemisinin-Piperaquine Drugs Using a Low-Cost Handheld near-Infrared Spectrometer." *Journal of Analytical Methods in Chemistry* 2022 (2022): 5335936.