B4 | OLD/NEW POLITICS OF ACCESS TO MEDICINES

Introduction

Mention the words "access to medicines" and one's mind is immediately cast back to the battles to make HIV/AIDS medicines available to people in Africa in the 1990s. But despite some significant wins, inequities in access have persisted over time and have been growing in importance in recent years due to the increasing number of high-cost technologies entering markets. The COVID-19 pandemic has brought urgent attention to solving the problem of inequitable access to pharmaceuticals, with the future of the world's 7.8 billion people dependent on affordable, timely access to new diagnostics, treatments, and vaccines.

In this chapter we explore the problem of inequitable access to medicines, the way it has changed over time, and the entrenched global power structures that perpetuate the status quo, including the power of the pharmaceutical industry. We examine the way in which intellectual property (IP) regimes allow for monopoly pricing and the exclusion of competition and trace the expansion of IP protections through trade agreements over the last two and a half decades. We also explore regulatory processes and the ways in which these can also limit access. Special attention is given to the global politics of access to COVID-19 products, efforts to provide timely and affordable access globally, and the persistent barriers encountered in meeting this aim. Throughout, current debates about how to make medicines more affordable, options that are being investigated, and the efforts of activists to change the status quo are described, and opportunities provided by the COVID-19 pandemic to reimagine how to provide access into the future are considered.

Inequities in access to medicines

Access to "safe, effective, quality and affordable essential medicines and vaccines for all" forms a core part of Target 3.8 under the United Nations Sustainable Development Goals (SDGs), and is seen as key to achieving universal health coverage and SDG Goal 3 ("Good Health and Well-being") (United Nations 2015). Access to medicines and vaccines is also important for meeting many of the other Goal 3 targets (such as Targets 3.3, "By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases," and 3.4, "By 2030, reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being") (United Nations 2015).

Over the last few decades, significant advances in medical technologies have seen large reductions in morbidity and mortality due to infectious diseases such as polio, HIV/AIDS, rotavirus, and hepatitis C, as well as non-communicable diseases including various cancers and autoimmune diseases (United Nations Secretary-General's High Level Panel on Access to Medicines 2016). For large parts of the world's population, however, lack of access to affordable medicines remains a significant problem. The World Health Organization (WHO) estimated in 2004 that almost 2 billion people did not have access to essential medicines (WHO 2004). In 2015, the WHO and the World Bank (2015) estimated that 400 million people were still missing out on access to medicines, vaccines, diagnostics, and medical devices. The report found that, globally, only 37% of people living with HIV had access to anti-retroviral treatment, while treatment coverage for hypertension ranged from 7%–61% of people with high blood pressure, with effective coverage ranging from 1%–31% (WHO and World Bank 2015). Large numbers of people also continue to go without treatment for neglected tropical diseases, which lack sufficient investment in research and development (United Nations Secretary-General's High Level Panel on Access to Medicines 2016).

A large proportion of those who lack access to medicines, vaccines, and other medical products live on low incomes in middle-income countries (ibid.). Middle-income countries, often referred to by the pharmaceutical industry as "pharmerging markets" (IQVIA Institute for Human Data Science 2019), can face steeply increasing tiered pricing arrangements that make it difficult to provide access for low-income groups; for example, increasing gross national income (GNI) per capita is associated with sharp increases in prices for vaccines (WHO 2018). For low-income countries, medicines account for the largest proportion of out-of-pocket care costs, with the proportion dedicated to medicines increasing as national income decreases (Vialle-Valentin et al. 2008). But people on low incomes in wealthy countries can also experience difficulties obtaining affordable access.

Gender equity with respect to access to medicines and vaccines has been little-studied as a global phenomenon, although gender differences in access are common when examining specific nations, treatments, and conditions (Stephens et al. 2013). Depending on the setting, women and girls' access to medicines can be limited by many factors other than socioeconomic status including gender discrimination, religious and cultural practices, lack of financial independence, and gender-based violence (Mike 2020).

Affordability as a key determinant of access

Access to medicines depends on many factors including financing, information systems, procurement and distribution systems, health service delivery, and human resources (United Nations Secretary-General's High Level Panel on Access to Medicines 2016). However, medicine affordability is crucial to achieving equitable access (Wirtz et al. 2017). An important historical case study is the lack of access to HIV/AIDS treatments in Africa in the 1990s. In 2000, HIV/AIDS

treatments costed more than $10,000 per patient per year until social struggles to provide access to generics in 2001 brought the cost down to a fraction of the original price thanks to the Indian generics producers' reaction to mounting mobilization around this piercing issue (Médecins Sans Frontières 2002).

In recent years, high-cost medicines such as cancer and immunotherapy treatments, along with treatments for hepatitis C, have seen rising pharmaceutical expenditure which has challenged the ability even of high-income countries (HICs) to provide access. In 2019, the global pharmaceutical market was predicted to be worth more than $1.5 trillion by 2023, growing at 3%–6% per year (IQVIA Institute for Human Data Science 2019). A 2015 Organization for Economic Cooperation and Development (OECD) report found that pharmaceutical expenditure, which accounted for approximately 20% of health expenditure in OECD countries in 2013, was continuing to rise, mainly driven by increasing numbers of high-cost medicines becoming available, some of which only provide minor improvements in comparison with existing drugs (OECD 2015). In 2015, the median price of a 12-week course of sofosbuvir, a breakthrough treatment for hepatitis C, was $42,017 across 26 OECD countries, with lower-income countries paying higher adjusted prices than higher-income OECD members (Iyengar et al. 2016). A cross-country study of access to medicines for cardiovascular disease found that these medicines were "unavailable and unaffordable for a

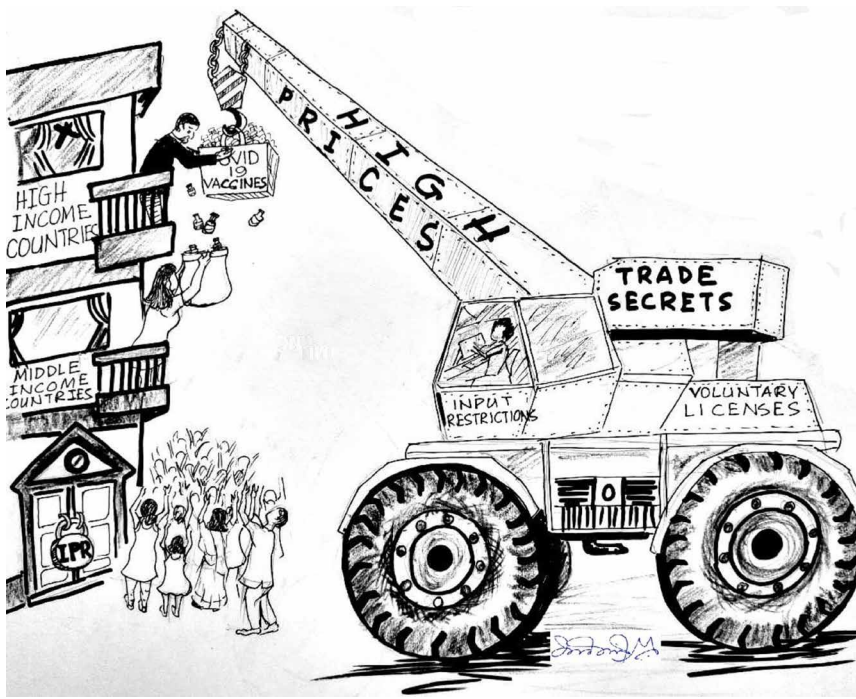

Image B4.1 Inequitable access to COVID-19 vaccines.
Source: Sketch by Indranil for *Global Health Watch 6.*

large proportion of communities and households in upper middle-income, lower middle-income, and low-income countries" (Khatib et al. 2016: 61). In many low- and middle-income countries (LMICs), particularly in South-East Asia and Africa, out-of-pocket spending on medicines is one of the main causes of catastrophic health expenditure (World Health Organization and International Bank for Reconstruction and Development 2020), with high prices acting as a barrier in any public provisioning of medicines in LMICs (Ewen et al. 2017).

Box B4.1: Colonial control: pharmaceuticals access in Palestine

Access to essential medicines, as part of the right to the highest attainable standard of health, is well founded in international law. This extends to ensuring the right of countries to develop their own pharmaceutical manufacturing capacity, which can grant long-term affordable access to essential medicines.

Pharmaceutical production in Palestine started in the West Bank and Gaza Strip in the 1970s. There are many Palestinian companies that produce pharmaceuticals for the local market and for export: Birzeit Pharmaceutical Company, Jerusalem Pharmaceuticals, Dar Al-Shifa Pharmaceutical Company (Pharmacare), Beit Jala Pharmaceutical Company, Sama Pharmaceuticals Manufacturing, Gamma (now closed), and Middle East (Megapharm) (Social and Economic Policies Monitor 2013, 54). These companies cover around 60% of the Palestinian market's pharmaceutical needs. They also export to Eastern Europe, Jordan, Algeria, Qatar, and Germany.

In its latest report, the Palestinian Authority's Ministry of Health revealed that it spends around 366 million Shekels on medicines, vaccines, laboratory supplies, and medical consumables, which constitutes 18% of its budget. The procurement of medicines from abroad constitutes around 40% of the Palestinian Authority's delayed payments (debt) budget line (around 336 million Shekels) (Palestinian Ministry of Health 2019, 70).

The regulation of the Palestinian pharmaceuticals market is subject to the Paris Protocol, which governs the economic and financial relations between "Israel" and the Palestinian Authority. The Protocol also regulates importing, exporting, and taxation mechanisms. This has led to the occupation government imposing restrictions on Palestinian pharmaceutical manufacturers, leading to the pharmaceutical market being flooded with competitively priced "Israeli"-produced medicines, undermining the local industry. The occupation government also slows the production process of Palestinian pharmaceutical companies by delaying imported needed raw materials allegedly to conduct security checks (Social and Economic Policies Monitor 2013, 54).

The occupation's Ministry of Health allows only medicines registered in "Israel" to be imported by the West Bank and Gaza Strip, denying

Palestine the ability to maintain pharmaceutical importing or exporting relations with its closest markets. Pharmaceutical products to which access is being prevented include inexpensive generic medicines manufactured in India and China, as imported medicines registered in "Israel" come mainly from the EU, North America, and Australia (Who Profits from the Occupation 2012).

Under agreements with the Palestinian Authority, "Israeli"-produced or imported medicines enter Palestine without the need to pay any customs, change their products, or change their product packaging. "Israeli" and multinational companies can sell medicines to Palestinians without having to provide any instructions in Arabic, and without considering different social categories based on income when drug prices are set.

This situation led to "Israeli" companies monopolizing the medicine manufacturing and distribution market in occupied Palestine while ignoring the human rights guidelines, with a huge increase in the capital of those companies. The outcome of these policies is a loss of Palestinian pharmaceutical manufacturing capacity.

In 2018, the value of imported medicines increased from the previous year and ranked seventh of the top ten products imported from "Israel" (Palestinian Central Bureau of Statistics 2019, 153). If the Palestinian Authority stopped importing pharmaceuticals from "Israel," local companies could increase their current level of coverage in the local market from between 50% and 60%, to between 70% and 80%. The Palestinian Authority will still need to import some medicines which are too costly to produce domestically or that require special production lines, but its ability to do so should not be confined to "Israeli"-registered products only and should not be at the cost of weakening its own domestic manufacturing.

Authors' note: We took the decision to write "Israel" in quotation marks because we, as Palestinian people, do not recognize the legitimacy of the "Israeli" state on the lands that have been colonized in 1948 by Zionist entities. Palestinian people have lived under colonization since 1948, under occupation since 1967, and under apartheid regime from the river to the sea for decades. We will never stop demanding the respect of our right to self-determination based on international law.

The COVID-19 pandemic: highlighting global inequities

The COVID-19 pandemic has starkly highlighted global inequities in access to medicines and vaccines and in access to other medical products such as devices and diagnostics. Trade in medical products was already highly concentrated and inequitable due to neoliberal policies disincentivizing local manufacturing, with the top ten importers, all HICs, accounting for 65% of the world's medical imports (including personal protective equipment and ventilators) in 2019 (World Trade Organization 2020a). Similarly, the top ten exporters of medical

products (all HICs except for China) accounted for 74% of exports (WTO 2020a). These inequities were exacerbated during the pandemic, with per capita imports of COVID-19 medical products in HICs exceeding those of low-income countries (LICs) by a factor of around 100 (United Nations Conference on Trade and Development 2020).

Early in the pandemic, the WHO along with several global health and private organizations (including the Bill & Melinda Gates Foundation) established the Access to COVID-19 Tools Accelerator (ACT Accelerator) to support the development and distribution of COVID-19 medical technologies (see Chapter D1). The ACT Accelerator includes four pillars: diagnostics, treatments, vaccines, and health systems strengthening. The vaccines pillar, COVAX, aimed to allocate at least 2 billion doses of vaccine equitably amongst participating countries according to population, providing 20% coverage by the end of 2021.

These mechanisms to promote affordable access have not attracted sufficient investment: by June 2021 the ACT Accelerator was $16 billion short of its funding targets (Business Standard 2021), and by the end of August 2021 COVAX had shipped less than 230 million vaccine doses (UNICEF n.d.), putting it way behind its goal of delivering 2 billion by the end of the year. Meanwhile, by November 15, 2020, governments had negotiated pre-purchase agreements directly with pharmaceutical companies for almost 7.5 billion doses of COVID-19

Image B4.2 Inequitable distribution of COVID-19 vaccines.
Source: Sketch by Indranil for *Global Health Watch 6.*

vaccines, 51% of which had been reserved by wealthy countries representing only 14% of the global population (So and Woo 2020).

This imbalance has only worsened over time. On August 4, 2021, the director general of the WHO pointed out that "So far, more than 4 billion vaccine doses have been administered globally. More than 80% have gone to high- and upper-middle income countries, even though they account for less than half the world's population" (WHO 2021). By this stage, while HICs had administered close to one dose per person on average, low-income countries had only managed to administer 1.5 doses per 100 people (WHO 2021). Many HICs have begun stockpiling reserves for booster programs, ignoring an appeal by the WHO for a moratorium on booster shots until health workers and older adults could be vaccinated in all countries (The Straits Times 2021). G7 countries are expected to have close to a billion stockpiled vaccine doses left over by the end of 2021, even after completing their booster programs (Lovett 2021).

This inequitable distribution of COVID-19 vaccines could greatly slow the global recovery from the pandemic. A study undertaken by researchers at Northeastern University (Chinazzi, Davis et al. 2020) modeled two vaccine distribution scenarios based on the hypothetical case of 3 billion doses of a single dose vaccine available on March 16, 2020. The first (uncooperative) scenario assumed the first 2 billion doses would be reserved for HICs with the remaining billion distributed equitably according to population. The second (cooperative) scenario involved equitable sharing of all 3 billion doses according to population. For a vaccine of 80% effectiveness, they found that the cooperative strategy would avert 61% of deaths by September 1, 2020, while the uncooperative strategy would only avert 33%. Estimates of the global economic costs of vaccine nationalism by the RAND Corporation (Hafner et al. 2020) and the International Chamber of Commerce (Cakmakli et al. 2021) found that hoarding of vaccines by wealthy countries could result in a gross domestic product (GDP) loss to the global economy of around $1.2 trillion (in GDP terms) and between $1.5–$9.2 trillion respectively.

The global intellectual property regime and its effects on access to medicines

One of the root causes of inequitable access to medicines and vaccines is the global regime of intellectual property rights (IPRs) for pharmaceuticals. Intellectual property rights provide a period of exclusivity where the rights holder can prevent third parties from making or selling the product. The rationale for providing these exclusive rights is to offset the high development cost and provide incentives for investment. However, arguments that IPRs and monopoly pricing are necessary to incentivize innovation are not supported by sound evidence – in fact, there is evidence to suggest that intellectual property can hamper drug development (Government Accountability Office 2006). Estimates of research and development (R&D) costs are often based on non-transparent industry information from confidential surveys or proprietary databases and vary widely,

from the low hundreds of millions to close to a billion dollars per new discovery (Morgan et al. 2011). Much of the R&D that results in new drugs is publicly funded (Galkina Cleary et al. 2018) and prices of new drugs are often set so high they generate income that greatly exceeds the likely R&D costs (Tay-Teo et al. 2019). Increasing IPRs has not been shown to incentivize innovation or increase technology transfer in LMICs (Sweet and Eterovic Maggio 2015) or to give rise to greater R&D for diseases that mainly affect the Global South (Kyle and McGahan 2012).

The global IPR regime is underpinned by the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), established in 1995, which set into place an agreed minimum standard for IPRs for all members of the World Trade Organization. These IPRs included a minimum 20-year patent term for both product and process patents in all fields of technology, including pharmaceuticals. The TRIPS Agreement represented a profound change. Prior to TRIPS, countries had varying patent periods, with many LMICs not providing patent protection at all, or at least not for pharmaceuticals ('t Hoen 2009). The negotiation of TRIPS involved intense lobbying by the pharmaceutical industry and HICs and opposition by many LMICs, which ultimately agreed to adopt TRIPS in the vain hope that it would reduce unilateral trade retaliation over perceived IPR breaches from the US ('t Hoen 2009). As Peter Drahos describes, "TRIPS was the outcome of a sophisticated networked power wielded by a coalition of powerful developed states and corporate actors seeking greater economic rents for their intellectual property assets" (Drahos 2007, 12).

Over the last 25 years, the TRIPS Agreement has legally prevented manufacturing of generic pharmaceutical products and has legitimized private ordering of pharmaceutical production and supply in low- and middle-income countries (LMICs). TRIPS, however, does provide certain flexibilities to allow members to meet the public health needs of their populations, thanks to the relentless efforts of some countries in the Global South during the General Agreement on Tariffs and Trade (GATT) negotiations (particularly India and Brazil). The rights of World Trade Organization (WTO) members to use these flexibilities were re-affirmed in the Doha Declaration on the TRIPS Agreement and Public Health adopted in 2001 (World Trade Organization 2001). One of these flexibilities is compulsory licensing, which allows for a patented invention to be exploited without the permission of the patent holder in certain circumstances. While this remains an important mechanism for enabling access, in the two and a half decades since TRIPS compulsory licensing has remained relatively little-used, mainly limited to HIV/AIDS drugs (Son and Lee 2018), with countries that do invoke their right to use it facing pressure from the USA, the EU, and other wealthy countries (Navarro and Vieira 2021).

In the meantime, bilateral and regional trade agreements negotiated outside of the WTO umbrella have incrementally added to the IPRs enshrined in TRIPS, lengthening patent terms, expanding the scope of patentability, and adding

further layers of IP rights that delay generic competition (see Chapters C3 of *Global Health Watch 3* and D4 of *Global Health Watch 4*). This is particularly the case for trade agreements negotiated by the United States and the EU, where most of the transnational pharmaceutical corporations are headquartered (Lopert and Gleeson 2013).

IPRs commonly sought by the US in its trade agreements include patent term extensions, data exclusivity (exclusivity for test data are submitted to regulatory agencies for the purpose of obtaining marketing approval), patents for new uses, processes, and/or methods of using known products, and patent linkage (creating a dependent relationship between patent status and marketing approval) (Lopert and Gleeson 2013). These IPRs all appeared in the Trans-Pacific Partnership Agreement (TPP) (Gleeson et al. 2018) and then subsequently in the United States-Mexico-Canada Agreement (USMCA) (Labonté et al. 2019), at least until it was renegotiated and amended to get it through the US Congress, when some TRIPS-Plus provisions were altered or removed (Labonté et al. 2020). EU agreements have included a similar set of IPRs; for example, the Comprehensive Economic and Trade Agreement (CETA) between the EU and Canada included data exclusivity provisions along with an additional period of protection following the end of the patent term (Lexchin and Gagnon 2014).

The pharmaceutical industry has lobbied heavily for increased IPRs in these trade agreements. This is particularly notable in the USA, where the industry associations and pharmaceutical companies have direct input to the US trade negotiating positions through its formal trade advisory committees, as well as exercising influence through other avenues including political donations and close informal relationships with trade negotiators (Gleeson et al. 2017).

The IPR expansionist agenda has not gone unopposed; significant civil society movements have countered the pharmaceutical industry lobbying which has mitigated US and EU agendas and, in some cases, completely overturned them. The US and EU proposals have also met with resistance from other countries. In the TPP negotiations, the initial US proposals were mitigated significantly during the negotiations and when the Trump administration withdrew the USA from the agreement in 2017, the remaining parties suspended many of the TRIPS-Plus IPRs from the re-named Comprehensive and Progressive Agreement for Trans-Pacific Partnership (Pusceddu 2018). After the USMCA was signed, the agreement was renegotiated to ensure it obtained enough support from Democrats to be ratified by the US Congress. The amendments included removal of the controversial provision for extended exclusivity for biologics, along with removal or modification of several other TRIPS-Plus provisions (Labonté et al. 2020).

IPRs as barriers to access for COVID-19 products

During the COVID-19 pandemic, IPRs have created barriers to the rapid scaling up of treatments and vaccines. In the early stages, patents on N95 masks

threatened to prevent sufficient numbers being manufactured (Watkins 2020). Later, patents on the potential COVID-19 treatment remdesivir, together with restrictive licensing practices by its maker Gilead Sciences, prevented middle-income countries from accessing either the highly priced originator product, or the lower-priced version made by licensed manufacturers in India, Pakistan, and Egypt (see Box B4.1).

Voluntary efforts to facilitate sharing of IP such as the COVID-19 Technology Access Pool (C-TAP), established by the WHO following a proposal by Costa Rica (WHO 2020a), have largely failed to gain support from high-income countries and pharmaceutical companies. By the end of August 2021, C-TAP was supported by only 43 countries (almost all LMICs), but not by a single research-based biopharmaceutical company. At the time of writing, C-TAP remained unused. While some pharmaceutical companies have made voluntary promises to share IP during the pandemic, most have not, and with the notable exception of AstraZeneca, many clearly intend to profit from the COVID-19 products they make. Moderna, maker of one of the first COVID-19 vaccines to finish Phase III trials, issued a statement indicating that:

> … while the pandemic continues, Moderna will not enforce our COVID-19 related patents against those making vaccines intended to combat the pandemic. Further, to eliminate any perceived IP barriers to vaccine development during the pandemic period, upon request we are also willing to license our intellectual property for COVID-19 vaccines to others for the post pandemic period. (Moderna 2020, para. 3)

This statement was greeted with skepticism by some civil society organizations, who expressed reservations about the value of Moderna's commitment not to enforce patents given that it made no commitment to sharing the other types of information and resources that would be needed to make its vaccine (HealthGap 2021).

Despite large injections of public funding (Martin and Jani-Friend 2021), pharmaceutical companies hold the rights to determine who can access vaccines that are desperately needed the world over, and on what terms. According to Médecins Sans Frontières (2020a), the development and manufacturing of the six most promising vaccine candidates attracted $12 billion in public funding. The KENUP Foundation (2021) estimated that by January 2021, 93 billion euros of public financing (including advance market commitments) had been invested in COVID-19 vaccines and treatments, with over 95% of this amount devoted to vaccines. Yet some pharmaceutical companies are expected to profit handsomely from COVID-19 vaccines. Makers of two of the front-runner vaccines, Pfizer/BioNTech and Moderna, indicated in March 2021 that they expected to generate $15 billion and $18.4 billion in revenue respectively in 2021 based on existing supply agreements (Kollewe 2021, 6 March). By the end of July 2021, Pfizer was predicting COVID-19 sales worth approximately $33.5 billion for 2021, including expected sales of booster shots (Hopkins and Grossman 2021).

Box B4.2: IP and barriers to access during the COVID-19 pandemic: the example of remdesivir

Remdesivir was a candidate for COVID-19 treatment which appeared promising in the early months of the pandemic and was given emergency use authorization in some countries for severe cases of COVID-19. WHO later issued a recommendation against its use in hospitalized patients due to lack of evidence that its use reduced mortality and other significant outcomes (WHO 2020b).

Gilead Sciences, a US company, owns patents for remdesivir in more than 70 countries (Médecins Sans Frontières 2020c). For a five-day course of treatment (six vials), it set the price at $2,340 for US government buyers and purchasers in other high-income countries (Gilead Sciences 2020). The cost of production has been estimated at around $1 per day, or $6 for a full treatment course (Hill et al. 2020). The development of the drug was underpinned by at least $70.5 million in public funds (Public Citizen 2020).

Gilead negotiated voluntary licenses with pharmaceutical companies in India, Pakistan, and Egypt to produce the drug much more cheaply (Silverman 2020). One company, Cipla, planned to sell the drug for $66 dollars per vial (Reuters Staff 2020). But the terms of the licenses limited exports of these cheaper versions to 127 mainly low-income countries (Maybarduk 2020). Many middle-income countries – such as China, Brazil, and Mexico, for example – along with high-income countries were excluded from the deal.

The US government bought up almost all of the first three months' supply of remdesivir from Gilead (U.S. Department of Health & Human Services 2020), leaving many countries unable to source the drug from Gilead, and prohibited from either making it or sourcing it from other suppliers.

Some companies producing COVID-19 medical products have negotiated voluntary licenses with other manufacturers. However, these licenses are commercial contracts which are often non-transparent and can tightly restrict what companies with these licenses can do with the product, including how much they can manufacture, who they can sell or export it to, and for what price (Médecins Sans Frontières 2020b).

1. The TRIPS waiver for COVID-19 products

In October 2020, India and South Africa made a proposal to the WTO TRIPS Council that IPRs for COVID-19 products should be waived for the duration of the pandemic (WTO 2020b). This waiver would enable WTO members to elect to declare that their IP laws would not apply to COVID-19 products during the pandemic, thus paving the way for increased manufacturing of critical tools to

fight the pandemic (Dhar and Gopakumar 2020). While WTO members can use compulsory licensing to bypass patents, it is a time-consuming, cumbersome, and contestable mechanism. Compulsory licensing also only applies to patents, whereas several other IPRs, such as trade secrets protection, can block access to biologic treatments and vaccines by preventing competitors from accessing information about manufacturing processes, discussed later in this chapter, and biological resources such as cell lines (Levine 2020).

By March 2021, the TRIPS waiver had gained the support of more than 100 of the WTO's 164 member states but was blocked from moving to text-based discussions by the opposition of several wealthy countries including the USA, the European Union, the United Kingdom, Japan, Canada, Switzerland, Brazil, and Norway (Third World Network 2021).

In May 2021, the USA made an historic move in declaring its support for a waiver limited to vaccines (Office of the United States Trade Representative 2021). This development makes the success of negotiations for a waiver far more likely; several of the opposing countries have since fallen in line with the USA, although the EU continues to express the lack of need for such a waiver. It is not clear how long text-based waiver negotiations may take, although the new WTO Director-General is hoping for a consensus to be reached by November 2021.

Meanwhile, wealthy countries that have opposed the TRIPS waiver have continued to hoard vaccines and, in some cases, squabble over preferential access. In January 2021 the EU, facing supply shortfalls of the Pfizer/BioNTech and AstraZeneca vaccines, introduced regulations requiring export notifications and threatened to introduce export bans (Lee 2021). France and Germany made legal threats against AstraZeneca after production problems reduced its promised supply for the first quarter of 2021 by 75% (Boffey 2021). The underlying issues for the shortages – monopolies over the IP and production of the vaccines – are the very issues that the TRIPS waiver is intended to assist in addressing.

Some of the short-term access problems for COVID-19 products could be addressed through the TRIPS waiver along with incentivizing or requiring pharmaceutical companies to contribute to mechanisms for sharing knowledge and data (such as C-TAP) and investing in technology transfer and local production in LMICs. In the longer term, greater attention needs to be given to more fundamental changes to the way in which R&D is funded and to shifting the entrenched power imbalances that reinforce the status quo. Alternative mechanisms that have been proposed for funding R&D in ways that promote rather than obstruct access include financial incentives like grants and prizes, and other incentives to invest in R&D, along with shared licensing mechanisms such as patent pools, as discussed in Chapter B5 of *Global Health Watch 2*. A global R&D treaty, as called for by many civil society organizations and recommended by the WHO Consultative Expert Working Group (CEWG) on Research and Development: Financing and Coordination (2012), would help to ensure a more equitable distribution of the costs and rewards of pharmaceutical

R&D. Shifting power away from industry also requires improving transparency in pharmaceutical markets, to ensure that information about prices, sales, marketing expenditure, public financing, and so on, which is currently considered commercial-in-confidence, is available to governments and the public. Building support for these types of initiatives in the face of trenchant opposition by the pharmaceutical industry requires civil society action, as in the case study of Universities Allied for Essential Medicines described in Box B4.3.

Box B4.3: Universities Allied for Essential Medicines UK: public return for public investment

Universities Allied for Essential Medicines (UAEM) is a student-led movement based at university campuses across 20 countries. We see universities as key to reimagining an innovation system that is fair for all. Up to a third of new drugs originate from public sector research, and universities are critical to the scientific progress underlying advances in health (Nayak et al. 2019). UAEM is therefore advocating for universities to implement equitable research and technology transfer policies that ensure affordable access downstream. In spring 2020, UAEM UK gathered online to foster a new generation of student campaigners. We experienced first-hand how grassroots activism can flourish during a pandemic, even when there is no physical space to come together and organize.

UAEM grew out of the HIV/AIDS crisis in the early 2000s, when students and staff at Yale University, supported by Médecins Sans Frontières, campaigned successfully against the prohibitively high price of the essential antiretroviral stavudine, developed at the university (Kapczynski et al. 2005). At the time 95% of HIV-infected people in the developing world did not have access to antiretroviral therapy. Following protests, the university was pressured to renegotiate the license with Bristol-Myers Squibb, which enabled a 30-fold drop in price. UAEM grew globally from this experience, focusing on improving technology transfer policies of publicly funded research institutions. Following advocacy efforts by UAEM students, Johns Hopkins University in the USA licensed the tuberculosis drug sutezolid to the Medicines Patent Pool (UAEM 2015).

At the start of the current pandemic, we recognized the need to invigorate our member base to tackle anticipated access challenges around COVID-19 health technologies, including drugs, vaccines, and diagnostics. The student body is a powerful voice within the university and can advocate for change at institutions otherwise inaccessible to other health activists. University-level decisions regarding technology transfer can impact the lives of millions of people downstream following transfer of a health technology to the private sector. We trained teams across the UK in the fundamentals of university

technology transfer, campaigning strategy, and creative activism, empowering students to address policies and practices at their own institutions. The first year of the pandemic also saw the finalization of the Equitable Technology Access Framework (ETAF) (UAEM 2020). This policy guidance framework aims to support universities in adopting policies for global equitable access and affordability of biomedical innovation. In collaboration with a local UAEM chapter, we saw the University of Edinburgh in December 2020 update its essential medicines policy as outlined in the ETAF framework. We hope to further expand the implementation of ETAF across higher education institutions in the UK.

To track the amount of public funding pledged towards COVID-19 R&D at universities, UAEMers from 15 countries collected and visualized this information on the interactive website *publicmeds4covid*. The Tracker illustrates that the public are the key investors and risk-takers for COVID-19 innovation, supporting the argument against upholding intellectual property rights and profit-making during the pandemic. For example, the British government, through direct research grants to universities and research institutions, spent approximately $169 million on the development of diagnostics, vaccines, and therapeutics for COVID-19 (UAEM 2021). A team of UAEM UK students also found that the research behind the Oxford-AstraZeneca vaccine was 97% publicly funded (Cross et al. 2021). Undertaking these research projects provided us with data to support our advocacy efforts, allowed us to challenge ideas about the origins of innovation, and strengthened our negotiation position with individual universities.

With many access issues being decided on a (inter)national level, we continued fostering our collaboration with other civil society organizations in the Missing Medicines Alliance (https://missingmedicines.org/) and the People's Health Movement. We mobilized young activists' voices for issues such as the COVID-19 Technologies Access Pool (C-TAP) and the TRIPS waiver proposal, as well as informing national debates in the UK Parliament on access to COVID-19 technologies (UAEM UK 2020). In collaboration with the Free the Vaccine Campaign and Act Up London, we organized a socially distanced protest to call for COVID-19 vaccines, drugs, and diagnostics to be sustainably priced, available to all, and free at the point-of-delivery.

If we are to achieve health equity worldwide, we need fundamental reform of the biomedical innovation system so that it puts people over profit, and we believe that student grassroots advocacy is part of this solution.

Image B4.3 The Free the Vaccine Campaign Carnival March in London on July 27, 2020, supported by UAEM UK student activists.

Source: Photo by Poppy Hosford, member of UAEM UK.

Regulatory regimes that constrain access to medicines

1. Industry involvement in international regulatory standard-setting processes

While the quality of medicines is critical to ensure the credibility of the health system, the norms and standards related to quality, safety, and efficacy (QSE) of medicines are not free from conflicts of interest. These norms and standards are being used by the research-based pharmaceutical industry to manage competition in the market.

> The primary forum for norms and standards setting related to QSE is the multi-stakeholder platform known as the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). The ICH was established in 1990 as a public–private partnership primarily to reduce development costs and hasten marketing approval processes for pharmaceuticals (Lexchin 2012). It has been criticized for lowering marketing approval standards for new chemical entities and for setting standards in a way that builds a set of technical barriers to prevent competition from the generic industry (Ohno 2002).

The founding members of ICH are the drug regulatory authorities of the EU, Japan, and the USA, and the research-based pharmaceutical industry associations of those countries. Prior to 2018, the steering committee of ICH, its highest decision-making body, constituted these founding members along with the International Federation of Pharmaceutical Manufacturers Associations (IFPMA, a federation of national associations of research-based pharmaceutical industry associations), WHO, Health Canada, and the European Free Trade Area. Only the founding members enjoyed voting rights. Until recent years, the ICH secretariat operated from the office of IFPMA (Nagarajan 2014).

In 2018, the governance mechanism of ICH underwent reform, and the steering committee was replaced with a 14-member management committee which included, along with the six founding members:

- two standing regulatory members (Health Canada and Swissmedic);
- two Standing Observers (IFPMA and WHO);
- regulatory agencies from Brazil, Singapore, the Republic of Korea, and China; and
- two industry associations, the International Generic and Biosimilar Medicine Association and Biotechnology Innovation Organization (BIO).

The research-based pharmaceutical industry remains firmly embedded in the decision-making structures of ICH. Further, until 2018 there was no representation of the generic medicines industry. ICH's role in norms and standards setting therefore raises serious concerns regarding conflicts of interest and accountability. As per its mission statement, the aim of ICH is to harmonize various technical and scientific aspects of pharmaceutical registration. While the word harmonization sounds attractive, harmonization of QSE norms and standards bears the dangers of compliance costs and impacts on the prices of medicines. The ICH initiatives have often resulted in the ratcheting up of the QSE norms and standards in ways that benefit the big firms and the members of ICH, at the expense of smaller or publicly funded firms and patients (Berman 2012). This concern was shared by a committee appointed by WHO to examine the impact of ICH guidelines in non-ICH countries which found that:

> In many countries, essential drugs required for the prevention and treatment of locally endemic conditions are not supplied by the major multinationals, but by local industry or by generic manufactures. If these suppliers are unable to meet what may be unsubstantiated quality standards, adverse impact of the withdrawal of these drugs on the population might well be far more dramatic than of any hypothetical risk posed by failing to achieve the ICH standards. (WHO 2002)

In short, the ICH standards set high standards claiming to protect patients but have limited "clinical relevance" (Timmermans 2004).

In 2014 there was an attempt to mainstream the ICH standards through a World Health Assembly resolution on regulatory system strengthening for medical products (WHO 2014a). The draft resolution urged member states to follow ICH guidelines and to implement the guidance of international harmonization initiatives such as the Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (Gopakumar 2014). While direct references to ICH and harmonization were removed from the draft due to opposition from many low- and middle-income WHO member states such as India, harmonization efforts continue, and may be used as a tool to manage competition. Another example of legitimization of ICH is WHO's criteria for a stringent regulatory authority.

The WHO's observer role in ICH and the adoption of ICH norms and standards as part of WHO's advice to member states undermines the organization's integrity, independence, and credibility. Further, it violates the principles of WHO's Framework on Engagement with non-State Actors (FENSA) which states that any engagement with such actors must "protect WHO from any undue influence, in particular on the processes in setting and applying policies, norms and standards" (WHO 2016).

2. Regulatory regimes for follow-on biologics

Access to biologic products (including biotherapeutics and vaccines) is becoming critical due to their use in treating diseases such as cancer and autoimmune disorders, and the development of novel therapies and vaccines to address emerging diseases such as COVID-19. These products can be very expensive and there is a need to bring cheaper follow-on versions to market as soon as possible. However, there are formidable barriers to doing so, including international guidelines for assessing safety and efficacy.

When considering an application for marketing approval for a generic small molecule medicine, regulatory agencies primarily assess bioequivalence, i.e., whether a competitor's generic product is an identical copy of the originator. Therefore, a manufacturer of a generic medicine need not prove the safety and efficacy of the medicine through clinical trials, and instead can rely on the data produced by the originator to obtain marketing approval (once any period of exclusivity on the test data has expired). This means the generic medicine can be produced much more cheaply than the originator. For biologics, however, which are much more complex, the assumption is that the manufacturing process is critical in determining the clinical properties of the drug and therefore a follow-on product developed through a different manufacturing process (which cannot be an identical copy and therefore is referred to as a "biosimilar") needs to have its safety and efficacy established through extensive clinical trials. Since the originators protect their knowledge about the manufacturing process through trade secret protections and are not required to share information about the manufacturing process and the cell lines in the public domain, the competitor is

forced to depend on a different manufacturing process. In the absence of access to the originator's manufacturing process, which is protected as a trade secret, the competitor must use independently developed manufacturing processes and carry out clinical trials to prove safety and efficacy, which requires time and resources and makes the development process costly.

The WHO (2009) Guidelines on Evaluation of Similar Biotherapeutic Products (SBP) provide guidance on how to develop a non-originator product with a smaller number of clinical trials than those required for originator biologics. These guidelines, which set the norms for the marketing approval of biotherapeutics, are based on outdated precautionary assumptions and put onerous requirements on their assessment, creating entry barriers. Many scientists have questioned the science behind the requirements and have asked the WHO to reconsider the need for such extensive clinical trials for follow-on biotherapeutics (New 2019). In 2014 the World Health Assembly adopted Resolution WHA 67.21 (WHO 2014b), which requested the director-general to convene an expert committee to update the 2009 guidelines in the context of technological advances and national regulatory needs and resources. It wasn't until 2020 that this expert committee finally decided to revise the SBP guidelines (WHO 2020c). Meanwhile, the lack of competition in the biosimilar market due to outdated regulatory barriers has compromised affordable access in LMICs. Currently, Canada, the EU, and the USA account for 77% of the market for monoclonal antibodies (the largest class of biotherapeutics), while the Asian Pacific accounts for 16%, Latin America 4%, the Middle East 2%, and Africa only 1% (International AIDS Vaccine Initiative 2021).

In the case of vaccines, there is no regulatory pathway currently existing to obtain marketing approval for a non-originator vaccine. As a result, every competing manufacturer is treated as a new vaccine developer and must carry out extensive clinical trials. If this regulatory insistence on clinical trials is not re-examined in the light of developments in science and technology, it risks using the façade of safety and efficacy concerns to stifle competition, thereby eliminating the possibility of affordable vaccines. The COVID-19 pandemic highlights the urgent need to explore reforming the regulatory framework to establish an approval pathway for non-originator vaccines.

3. Targeting of regulatory processes in trade agreements

Regulatory processes for pharmaceuticals, including the assessment of safety, efficacy, and quality, along with procedures for pricing and reimbursement, have increasingly been targeted in recent trade agreements, particularly those negotiated by the USA (Gleeson et al. 2019). The Australia–US Free Trade Agreement (AUSFTA) which came into force in 2005, for example, saw provisions targeting national coverage programs for pharmaceuticals introduced in a trade agreement for the first time. Similar provisions have since appeared in the Korea–US Free Trade Agreement (KORUS), the TPP (before the USA withdrew

from it), and the USMCA. While varying between agreements, these provisions generally impose detailed procedural requirements in the pharmaceutical industry's favor, including time limits for assessing proposals for listing drugs on national formularies, disclosure of decision-making criteria and reasons for decisions, and review or appeals processes for unsuccessful listing applications. Opportunities for industry input during decision-making and for consultation between trade partners about pharmaceutical policy must also be provided (Gleeson et al. 2019). These requirements raise concerns about the potential for reduced flexibility and industry interference in pharmaceutical decision-making and for pressure from trade partners such as the USA (Gleeson et al. 2019). These types of rules are generally unpalatable to other countries, as evidenced by the suspension of the procedural rules from the CPTPP after the collapse of the TPP. However, their inclusion in three US trade agreements in force (AUSFTA, KORUS, and the USMCA) suggests that its trade partners are in many cases prepared to accept them in exchange for access to US markets.

Recent US free trade agreements have also included provisions pertaining to marketing authorization processes and pharmaceutical inspections. The TPP and USMCA contain provisions seeking to harmonize processes for assessing safety and efficacy and align them with international standards; depending on how it is done, this may drive standards downwards or towards industry-favorable norms (Gleeson et al. 2019). These agreements also set criteria for making marketing authorization decisions, which may reduce flexibility and opportunities for requiring companies to submit data needed for transparency purposes, such as R&D costs or public financing received (Gleeson et al. 2019). Other provisions in these texts may increase pressure for accelerated decision-making about drug approval (with concomitant safety risks), protect information about pharmaceutical inspections from public disclosure, and encourage the participation of the pharmaceutical industry in the development of policies and standards (Gleeson et al. 2019).

Conclusion

There have been few times in history when inequities in access to medicines have seemed so stark, the health, economic, and social costs so high, and the underlying causes so intractable as in the case of COVID-19. We have traced in this chapter how the problem of inequitable access to medicines is underpinned by global intellectual property, trade, and regulatory regimes that stifle competition and allow medicines and vaccines to be monopolized by private companies and wealthy countries. After 25 years of WTO rules, with increasing proliferation of TRIPS-Plus rules and ongoing difficulties with using TRIPS flexibilities, the medicines access problem that at the beginning affected primarily the Global South has become a problem affecting wealthy countries as well. The power of the pharmaceutical industry in influencing norm and standard setting at the international level, as well as the behavior of individual nation states, is

long-standing and undeniable. Yet access to medicines activists and civil society organizations have continued to challenge and disrupt the status quo, with some important victories such as the Doha Declaration on the TRIPS Agreement and Public Health, the removal or mitigation of TRIPS-Plus provisions in many trade agreements, and the mobilizing of efforts to get approval at the WTO for the TRIPS waiver. Whether or not the TRIPS waiver campaign succeeds, there remains an urgent need for governments and activists to continue to challenge TRIPS and TRIPS-Plus intellectual property regimes, which deny new medicines to much of the world's population while protecting pharmaceutical industry profits in high-income countries. The COVID-19 pandemic and the negotiations taking place at the WTO for a TRIPS waiver for COVID-19 medical products provide opportunities for activists and civil society organizations to further advance the cause of access to medicines, potentially opening the space for more fundamental reforms and power shifts.

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