Patent Waiver: Globally Equitable Supply of Vaccines and the Relation to the US Pharmaceutical Industry

Shiyu Yan(✉)

Department of Economics, University College London, London, UK
laura.shiyuyan@gmail.com

Abstract. The request for a COVID-19 vaccine patent waiver since 2021 has raised worldwide concern due to the greater availability of vaccines among developed countries compared to the developing world. This paper analyses the pharmaceutical industry in the United States using a Porter's five forces model to shed light on the level of competition among the companies. This complements the following discussion over the proponents and opponents of patent waiver for the COVID-19 vaccines, which particularly emphasizes the macro factors regarding society, politics, economics, and technology, and strengths and opportunities for an individual firm. It then evaluates the existing cooperation and aiding schemes across countries to seek improvements in the distribution of vaccines. Finally, the conclusion draws on the potential of the structure of the medicine industry to affect the vaccine distribution, and calls for a more positive contribution from the advanced economies.

Keywords: Economics · Management · Patent Waiver · the US Pharmaceutical Industry · the Porter's Five Forces Analysis · TRIPS

1 Introduction

The COVID-19 pandemic since 2021 has already had a number of serious impacts on the global economy [1], including but not limited to a slow-down of GDP growth, supply chain disruption, surging unemployment, and business failures, that have led to a significant fall in living standards. Some previous studies have shown that getting vaccinated can reduce the mortality rate of COVID-19 to a great extent [2], yet the vaccine supply has been concentrated among economically more developed countries [3], which is also reflected by their higher vaccination ratio in the population [4]. This gives rise to an essential problem of vaccine inequality across countries, which has attracted the concern of global society. A joint proposal was put forward by India and South Africa in 2020 to waive off the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), for an equitable distribution and easy access to vaccines as public goods, which has amassed solid support from most developing countries [5].

The existing system has done much to safeguard the integrity of the intellectual property system from infringement, while sacrificing the economic interests of many

© The Author(s) 2022
G. Ali et al. (Eds.): ISEMSS 2022, ASSEHR 687, pp. 1053–1062, 2022.
https://doi.org/10.2991/978-2-494069-31-2_123

people who are in urgent need of these technologies when a real crisis hits. For instance, proposals were made by the Consultative Expert Working Group in 2012 to divorce the patent regime from some medicines for the diseases that has been typically affecting developing countries [6]. The aim is to refute the argument for monopoly pricing to recover Research & Development costs, and replacing it by an incentive mechanism. However, due to the reluctance of the United States and other developed countries, these proposals were still in pending. Factually, more effort should be contributed by the countries with higher productivity, rather than overspending on negotiation, in order to assist the underdeveloped countries in overcoming the crisis facing the entire human race. Global society should seek institutions and cooperation providing a better balance between the advanced economies in the North and the less developed in the South.

Using the background of the United States pharmaceutical industry, this paper essentially discusses the two opposing views on the patent waiver and the failures of the current vaccine aid programs. It provides an innovative way to explain the current uneven global distribution of vaccines associated with the market structure of developed pharmaceuticals, and calls for improvements to be made in the existing cooperation between North and South countries.

2 The Porter's Five Forces Analysis

2.1 Background

The Porter's five forces concept was first raised by Michael Porter in his work Competitive Strategy, which to a great extent determines the structure of all industries, and establishes the competition rules and the fundamental attributes of profitability within them. The five forces framework includes the threats posed by competitive rivalry, powerful buyers and suppliers respectively, potential new entrants, and substitute products. The analysis then comes to evaluate each source of threats and its driving factors. Furthermore, the five forces can be potentially used to indicate the strategic impacts of companies within an industry, such as the pivotal opportunities and challenges facing the organisation of concern [7].

The following paragraphs use a standard Porter's five force model to analyse the level of competition among the US branded drug companies, focusing on the current direct competitors, suppliers, buyers, new entrants into the industry, and indirect competitors.

The reason for using the US pharmaceutical industry typically as the background to evaluate the patent and the waiver is related to its own significance and the actions being taken by the firms and the Biden-Harris administration. The US owned the largest share of pharmaceutical sales over the past decade, at around 40–50%, which has taken the dominant position in the global market [8]. The health care sector accounted for 8.6% of the US GDP in 2020, along with education services and social assistance [9]. The US has about 3.3 million patents in force by 2021 [10], and has seen steady growth in the annual number of patents issued over the past two decades [11]. Pharmaceutical firms in the United States have been closely linked to patents, especially in terms of return on innovation. Furthermore, the healthcare industry has reached an agreement with the Obama administration on medical rebates and insurance in 2009 in order to obtain greater political assistance [12]. Known as one of the supporters of the US Democratic party, the

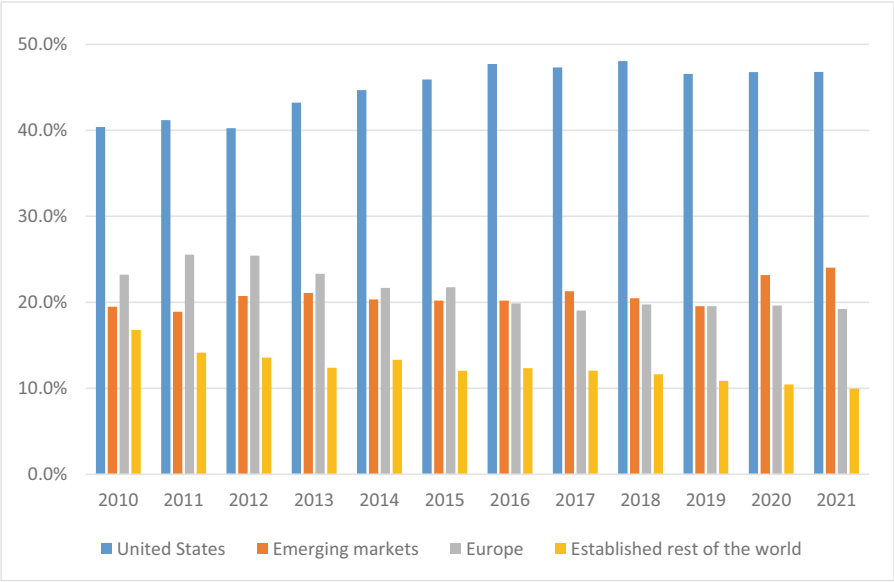

Fig. 1. World pharmaceutical sales 2017–2021 by region [8] (Mikulic, M. Global Pharmaceutical Sales by market 2017–2020. Statista, 2022, Licensed by the author)

interests of medicine-producing firms and the Democratic administration are entangled, causing the actions of one party to affect the other (Fig. 1).

2.2 Analysis

The existing level of competition among the branded pharmaceuticals has been moderate in the industry. Johnson & Johnson made 91 billion dollars in 2021, which nearly doubled the revenue of the second place, Pfizer Inc. (55 billion dollars) [13]. A general increasing trend has been observed in the weight of research and development costs in total revenue since 1990, mounting to over 20% in 2020 [14]. For a medicine to be relatively more effective, its R&D cost is usually higher, which pushes up the charges to consumers. Evidence also suggests that branded producers have been engaged in fierce non-price competition rather than lowering prices to obtain more consumers, such as spending billions of dollars on marketing and advertising, which has been accused of the attribution of excessive markup [15]. Such patterns of cost, revenue, and competition imply an oligopolistic market structure, as there are several large firms dominating the market who are capable of bearing high sunk costs.

The patent is regarded as a Pareto improvement to encourage innovation, which has a positive spillover effect. The incumbent firms can submit patent applications for their innovative products, which, if approved by a sovereign authority, grants the patent owner the unique power to use the technology for around 20 years. The firm will be made as a monopoly with significant market power to determine the price of the product incorporating the protected technology, thereby enabling to exploit huge economic benefits

as a reward for massive spending on R&D [16]. Therefore, patent is the incentive and award to innovation which virtually eliminates both existing and potential competition.

Apart from significant expenditure on research and marketing, many pharmaceuticals have outsourced drug production from countries like China to benefit from cheaper and more productive labour [17]. This indicates the big pharmaceuticals have greater bargaining power over its suppliers. However, the stability of the supply chain is subject to strategic changes in policies between the trading partners and other external factors affecting the sourcing countries, such as lockdown during the COVID-19 pandemic.

Despite the need as a necessity, demand for medicine kept rising as some consumers are willing to pay a higher price for better quality. In this case, features of a Veblen good are observed from brand-name drugs, making the demand to correlate positively with price. Additionally, medical staff, who provide the prescription to the general public, might not be aware of the relative prices of different drugs or have made tacit agreements with drug producers, resulting in their failure to provide the most cost-efficient treatment to the patients. Lakdawalla (2018) pointed out that a near-monopoly pricing model was observed in the uninsured market, whereas the firms had lower bargaining power against insurers in order to gain more popularity [18].

The industry has a number of barriers impeding potential new entrants, such as huge sunk costs on R&D and marketing, and the exclusive property right to produce a particular medicine. Sarpatwari et al. (2019) also found that new entrants did not necessarily drive down the price of brand-name drugs. However, the retail prices of the existing products helped restrict the launch price of the new drugs, suggesting that the consumer demand was more strongly shaped by the price anchors rather than their self-judgement or willingness to pay [19]. This may also hint at a tacit collusion in the form of price leadership between the incumbent firms and the new entrants.

Generic drugs are widely considered as a substitute for branded drugs, as they are bioequivalent to the branded products. Since the passage of the Hatch-Waxman Act in the mid-1980s, the demand for generic drugs has expanded rapidly, and almost approaching 90% in 2020 [20]. As market size increases, more producers are attracted as new entrants, leading to higher competition and lower prices of generic drugs. Saha et al. (2006) found that the ratio between generic and branded medicine has fallen, which was principally due to the surging number of suppliers of generic drugs that have brought down their price; yet slight decreases were noticed in the price of branded drugs resulting from the indirect competition [21]. A positive correlation between cost and price was also observed among generic drug producers. However, Ball et al. (2018) suggested that the cheaper products originated from lower production costs could indicate a deterioration in quality [22]. Additionally, there was a negative relationship between the number of existing firms and the rate of entrants, which was consistent with the prediction of the long-run markup model: the number of firms in a market and the markup for each firm will rest in an equilibrium in the long term [23].

3 The Reasons Behind the Support of the Patent Waiver

3.1 General Theory and Past Experience

Vaccines are merit goods that can generate positive external effect to the society. Theoretically, a population with higher vaccination rate exhibits greater productivity than a less vaccinated one, as they can build up stronger immune system against viruses and diseases. Empirically, getting more people vaccinated turns out to be an effective way to prevent the spread of a disease and the rise of a pandemic. Human beings have defeated smallpox virus for good in the 1980s via the invention of the specific vaccine [24]. During this pandemic, it has been proved that the death rate was five-times lower among the vaccinated individuals than the unvaccinated [25]. It is also proposed that the vaccines should be treated as public goods with features of non-rivalry and non-excludability to be made available regardless of purchasing power and improve economic welfare [26]. The temporary waiving of the TRIPS was proposed in order to seek borderless justice in rescuing COVID-19 patients, considering the monopolised vaccine supply in high-income countries and technical issues that are difficult for the underdeveloped countries to break through in the short run.

3.2 The US's Participation in Particular

By May 2021, there have been more than 100 countries and 250 civil society organizations urging support for the patent waiver of the COVID-19 vaccine [27]. The broad coalition of the waiver can reflect the keen desire for an early end to the pandemic and an international win-win situation. It is also suggested that the patent waiver can be a Pareto improvement to the current situation, as the economic gains from a quicker global recovery far exceed the loss of profit to the pharmaceuticals because of the waiver.

Meanwhile, the Biden-Harris administration expressed its support for an IP waiver for COVID-19 vaccines [28]. As mentioned in the Democratic Party's letter to Biden, this was an opportunity to reverse the damage to the international reputation of the US done by the Trump administration previously and retrieve their leadership in public health services on the global stage [29]. Another reason can be the surplus in the domestic supply: it has been condemned for wasting precious vaccines rather than donating to the low-income countries [30]. In a nutshell, the growing social concern has largely contributed to the actions of the current US administration, and it is likely to push the rest of the developed world forwards.

In terms of micro-economic aspects, complying with the appeal for vaccine patent waiver and showing social responsibility can earn opportunity and relative strength for a drug producer. According to Quezado et al. (2022), such behaviour can enhance competitive advantages and improve brand royalty for a firm to a great extent [31]. This is because it resonates with the value of the general public (potential or existing buyers) and the government, which are two important groups of stakeholders in a company [32]. Moderna has announced that it would not enforce COVID-19 related patents during the pandemic in 2021 [33]. It is reasonable to predict that its action aims at presenting a good image and building its reputation on this occasion, so as to pursue a larger market share, higher sales and profits in the future.

4 The Voice of the Opponents

Most pharmaceutical companies have been aggressively lobbying policymakers in the more economically developed nations to hold onto their objection to the patent waiver [34]. One of the reasons behind the opposition to the waiver is that the companies worry that the excuse of emergency or urgency would be abused, leading to the institution being undermined. Industries characterized by highly capital- and knowledge-intensive production, place significant value on the protection system of intellectual property rights due to the economic benefits its brings to further promote innovation. They could lose confidence in the authority and validity of the patenting institution, which can be interpreted as a worsening in the business environment, and hence become more reluctant to invest. A slowdown in the rate of investment will impede the capital stock accumulation of a country and thus potentially harm its economic development.

In addition, some opponents argue that low- and middle- income countries have been given a number of accesses to obtain more vaccines from overseas producers or to revoke IP during emergencies, including the Covax Facility, patent pools, compulsory licensing, and voluntary licensing.

The role of the Covax Facility is to raise funds for countries with less purchasing power to afford expenditure on vaccines, pledging to secure the basic amount of doses for these countries. However, huge uncertainty lies in such a promise. This is because future vaccine supplies have been locked up by large-scale bilateral advance purchase agreements and the willingness of the high income countries to invest in Covax has been draining. Several European countries have withdrawn from the Covax fund and turned to participating in advance purchase agreements sponsored by the EU [35].

C-TAP is regarded as a technology pool which aims at COVID-19 related know-how transfer in order to boost the invention of medical products. It focuses on data transparency and can possibly be made into a successful platform to collect technology and knowledge as "global public goods", which promotes a globally more equitable vaccine distribution. Nevertheless, the potential threat of an increasing number of open licensing has made the multinational companies which hold IP and the major countries reluctant to participate, which has led to their failure to realize such pooling so far [36].

Compulsory licensing is when a government or other legal authority permits a third party to use the subject matter of a patent without the authorization of the patent's holder [37], especially in the cases of national emergency, extreme urgency and public noncommercial use [11]. However, its flexibility has been criticized by some developing countries, including its time- and effort-consuming application process, and the product- and nation-specific approach it provided (rather than a global unanimous action to break the technology barrier during the COVID-19 pandemic).

Voluntary licensing is regarded as an appropriate method to promote generic drug production to improve medicine supply to the lower income earners, yet the contracts may include a number of limitations and may not exhibit a high degree of transparency [38]. Some companies have allowed voluntary licenses to some Asian producers in order to avoid compulsory licenses issued at the national level [39]. This is because the developers can at least receive some remuneration under the commercial terms of the specific contracts compared to the complete patent waiver. However, as argued by the

WHO, the terms of the voluntary license programs offered by some patent holders are insufficient to cope with the current epidemic [40].

Last but not least, it has been proposed that the overriding obstacle to global adequate and fair vaccine distribution lies in supply-side constraints in less developed countries rather than intellectual property barriers [41]. For instance, they lack sufficient funds to buy sophisticated medical equipment in scarce supply as well as well-trained labour to participate in vaccine production. In other words, they will not be able to produce enough vaccines even if they have access to the technology. However, supply-side expansion is a long term pursuit of a country requiring economic growth, a productive labour force, and consistent investment in infrastructure and R&D, which are unattainable for LDCs without recovery from the epidemic. Furthermore, the licensing can be granted to developing countries with a certain capacity for vaccine manufacturing, and thereby South-South cooperation can be encouraged [42]. For instance, South Africa has reported that they have nearly completed the reproduction of Moderna's COVID-19 vaccine without the collaboration of the developer, which was deemed as a crucial step in building capacity for vaccine manufacturing in the less developed countries [43]. As a result, the aiding programs should be adopted more quickly as a means of support for the residents in the LDCs to combat the virus in the short-run and achieve economic development in the long-run.

5 Conclusion

This paper uses a novel perspective to evaluate the current inequitable distribution of medical resources including vaccines at the global level. From the Porter's five forces analysis, it is shown that the competition level among the non-generic drug producers is negligible and it is difficult to promote competition in this industry. The near-monopolistic market position of these firms possesses them with a colossal amount of bargaining power, which then enables them to refuse to participate or enforce some international accords and limit vaccine access within high- and middle-income countries. However, this paper lacks quantitative analysis with the use of empirical evidence. Further research can focus on regressing practical statistics concerning pharmaceutical firms (such as sales, costs, wages, etc.) to supplement the Porter's five forces analysis; as well as the rules and collaborations seeking a better balance between the innovative sectors and groups with the most urgent needs, or more broadly, between the economically developed and less developed countries.

References

1. Jawad, M., Maroof, Z. & Naz, M., Impact of pandemic covid-19 on Global Economies (a seven-scenario analysis). Managerial and Decision Economics, vol. 42(7), 2021, pp. 1897–1908.
2. Roser, M. & Mathieu, E. Data on COVID-19 mortality by vaccination status, 2021. Online: https://ourworldindata.org/covid-deaths-by-vaccination#data-on-covid-19-mortality-by-vaccination-status.
3. Vaccine Tracker. Bloomberg, 2022. Online: https://www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/.

4. Ritchie, H. et al. Coronavirus (COVID-19) vaccinations, 2020. Online: https://ourworldindata.org/covid-vaccinations.
5. Singh, B. et al., Covid-19 and global distributive justice: 'health diplomacy' of India and South Africa for the trips waiver. Journal of Asian and African Studies, 2022.
6. World Health Organization, Consultative expert working group on research and development: financing and coordination. World Health Assembly, 2012, p. 65. Online: https://apps.who.int/iris/handle/10665/79197.
7. Dobbs, M. E., Guidelines for applying Porter's five forces framework: A set of industry analysis templates. Competitiveness Review, vol. 24(1), 2014, pp. 32–45.
8. Mikulic, M. Global Pharmaceutical Sales by market 2017–2020. Statista, 2022. Online: https://www.statista.com/statistics/272181/world-pharmaceutical-sales-by-region/.
9. BEA, US Department of Commerce. Percentage added to U.S. GDP by industry 2020. Statista, 2021. Online: https://www.statista.com/statistics/248004/percentage-added-to-the-us-gdp-by-industry/.
10. WIPO. Number of patents in force in the U.S. 2020. Statista, 2021. Online: https://www.statista.com/statistics/256738/number-of-patents-in-force-in-the-us/.
11. Gilbert, P. et al., Intellectual property rights and vaccines. Vaccine Design, 2412, 2022, pp. 505–518.
12. Spatz, I.D., Health Reform Accelerates Changes In The Pharmaceutical Industry. Health affairs, vol. 29(7), 2010, pp. 1331-1336.
13. Financial Times. 2021 ranking of top 10 U.S. biotech and pharmaceutical companies based on total revenue. Statista, 2021. Online: https://www.statista.com/statistics/257436/top-global-biotech-and-pharmaceutical-companies-based-on-revenue/.
14. PhRMA. Spending of U.S. pharmaceutical industry for research and development as a percentage of total revenues from 1990 to 2020. Statista, 2021. Online: https://www.statista.com/statistics/265100/us-pharmaceutical-industry-spending-on-research-and-development-since-1990/.
15. Waldman, P. Do Democrats have what it takes to stand up to the pharmaceutical industry? The Washington Post, 2021. Online: https://www.washingtonpost.com/opinions/2021/09/16/do-democrats-have-what-it-takes-stand-up-pharmaceutical-industry/.
16. Roberts, P.W., Product Innovation, Product–Market Competition and Persistent Profitability in the U.S. Pharmaceutical Industry. Strategic Management Journal, vol. 20, 1999, pp. 655–670.
17. Oehler, R.L. & Gompf, S.G., Shortcomings in the US Pharmaceutical Supply Chain: Potential Risks Associated With International Manufacturing and Trade-Related Tariffs. JAMA, vol. 324(2), 2020, pp. 143–144.
18. Lakdawalla, D.N., Economics of the pharmaceutical industry. Journal of Economic Literature, vol. 56(2), 2018, pp. 397–449.
19. Sarpatwari, A. et al., Competition and price among brand-name drugs in the same class: A systematic review of the evidence. PLOS Medicine, vol. 16(7), 2019, p. e1002872.
20. IQVIA. Proportion of branded versus generic drug prescriptions dispensed in the United States from 2005 to 2020. Statista, 2021. Online: https://www.statista.com/statistics/205042/proportion-of-brand-to-generic-prescriptions-dispensed/.
21. Saha, A. et al., Generic competition in the US Pharmaceutical Industry. International Journal of the Economics of Business, vol. 13(1), 2006, pp. 15–38.
22. Ball, G.P., Shah, R. & Wowak, K.D., Product competition, managerial discretion, and manufacturing recalls in the U.S. Pharmaceutical Industry. Journal of Operations Management, vol. 58–59(1), 2018, pp. 59–72.
23. Coreecon, Determinants of economic performance in the long run. The Economy. Online: http://www.core-econ.org/the-economy/book/text/16.html#determinants-of-economic-performance-in-the-long-run.

24. Diamond, J., Guns, germs and steel: the fates of human societies. W. W. Norton & Company, 2017, pp. 195–214.
25. Roser, M. & Mathieu, E. Why we need to compare the rates of death between vaccinated and unvaccinated. Our World in Data, 2021. Online: https://ourworldindata.org/covid-deaths-by-vaccination#why-we-need-to-compare-the-rates-of-death-between-vaccinated-and-unvaccinated.
26. Katz, I.T. et al., From vaccine nationalism to vaccine equity — finding a path forward. New England Journal of Medicine, vol. 384(14), 2021, pp. 1281–1283.
27. Johnson, J. 250 groups urge WTO chief to Ditch Pharma-friendly approach and embrace vaccine patent waiver. Common Dreams, 2021. Online: https://www.commondreams.org/news/2021/04/14/250-groups-urge-wto-chief-ditch-pharma-friendly-approach-and-embrace-vaccine-patent.
28. Office of the United States Trade Representative. Statement from ambassador Katherine Tai on the covid-19 trips waiver. United States Trade Representative, 2021. Online: https://ustr.gov/about-us/policy-offices/press-office/press-releases/2021/may/statement-ambassador-katherine-tai-covid-19-trips-waiver.
29. Johnson, J. To 'crush the virus,' majority of House Dems urge Biden to back vaccine patent waiver. Common Dreams, 2021. Online: https://www.commondreams.org/news/2021/05/04/crush-virus-majority-house-dems-urge-biden-back-vaccine-patent-waiver.
30. Eaton, J. & Murphy, J. America has wasted at least 15 million Covid vaccine doses since March, new data shows. NBCNews, 2021. Online: https://www.nbcnews.com/news/us-news/america-has-wasted-least-15-million-covid-vaccine-doses-march-n1278211.
31. Quezado, T.C.C., Fortes, N. & Cavalcante, W.Q.F., The Influence of Corporate Social Responsibility and Business Ethics on Brand Fidelity: The Importance of Brand Love and Brand Attitude. Sustainability, vol. 14(5), 2022, p. 2962.
32. Du, S., Bhattacharya, C.B. & Sen, S., Maximizing business returns to Corporate Social Responsibility (CSR): The role of CSR communication. International Journal of Management Reviews, vol. 12(1), 2010, pp. 8-19.
33. Moderna. Statement by Moderna on Intellectual Property Matters during the COVID-19 pandemic, 2020. Online: https://investors.modernatx.com/Statements--Perspectives/Statements--Perspectives-Details/2020/Statement-by-Moderna-on-Intellectual-Property-Matters-during-the-COVID-19-Pandemic/default.aspx.
34. Queally, J. 'Utterly Disgusting': Big Pharma Lobby Blitz Against Vaccine Patent Waivers Denounced. Common Dreams, 2021. Online: https://www.commondreams.org/news/2021/04/24/utterly-disgusting-big-pharma-lobby-blitz-against-vaccine-patent-waivers-denounced.
35. Ren, G., Massive mobilization of US $31.3 billion required for COVID-19 Diagnostics, Drugs & Vaccines accelerator. Health Policy Watch, 2020. Online: https://healthpolicy-watch.news/massive-mobilization-of-us-31-3-billion-required-for-covid-19-diagnostics-drugs-vaccines-accelerator/.
36. Chaudhuri, S., Making Covid-19 Medical Products Affordable: Voluntary Patent Pool and TRIPS Flexibilities. SouthViews, 2020, p. 200.
37. Bond, E.W. & Saggi, K., Compulsory Licensing and Patent Protection: A North-South Perspective. The Economic Journal, vol. 128(610), 2018, pp. 1157–1179.
38. Agarwal, H., Capitalizing an epidemic: Does voluntary license stabilizes access to patented vaccines and Public Health Crisis? The Journal of World Intellectual Property, vol. 24(5-6), 2021, pp. 455–467.
39. Steele, C. The Biden administration supports waiving patents on coronavirus vaccines. Big Pharma won't be happy. The Washington Post, 2021. Online: https://www.washingtonpost.com/politics/2021/05/05/biden-administration-supports-waiving-patents-coronavirus-vaccines-big-pharma-wont-be-happy/

40. Palmer, D., Poor countries are fighting with drug companies over vaccines. Now Biden must pick a side. POLITICO, 2021. Online: https://www.politico.com/news/2021/03/21/coronavirus-vaccine-wto-477272.
41. Storz U., The Patent Maze of covid 19 vaccines. Expert opinion on therapeutic patents, vol. 31(12), 2021, pp. 1177–88.
42. Legge, D.G. & Kim, S., Equitable access to covid-19 vaccines: Cooperation around research and production capacity is critical. Journal for Peace and Nuclear Disarmament, vol, 4(sup1), 2021, pp. 73–134.
43. Maxmen, A. South African scientists copy Moderna's Covid Vaccine. Nature News, 2022. Online: https://www.nature.com/articles/d41586-022-00293-2.

Open Access This chapter is licensed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (http://creativecommons.org/licenses/by-nc/4.0/), which permits any noncommercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license and indicate if changes were made.

The images or other third party material in this chapter are included in the chapter's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the chapter's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder.