PATENTS

What the COVID-19 pandemic revealed about intellectual property

The COVID-19 pandemic dispelled some myths underlying intellectual property policy and revealed how stakeholders can develop policies to accelerate development and ensure access using existing tools and experimenting with open science.

The COVID-19 pandemic challenged key assumptions underlying intellectual property (IP) policy, finding them wanting. During the pandemic, intellectual property (IP) was not a significant driver of innovation[1,2]; instead, it contributed to limiting and then delaying global access to vaccines and drugs[3–5]. Although companies played a critical role in vaccine and antiviral development, they financed their work through the prospect of large procurement contracts rather than the prospect of IP. Procurement, together with early stage funding, came largely from government.

Two myths surrounding IP delayed achieving the goal of rapidly delivering vaccines and antivirals equitably around the globe. The first is that without IP — specifically patents — there would have been no vaccines or drugs. The second is that IP in all its forms presents no significant barrier to global distribution of vaccines and antivirals. Neither myth accords with the evidence.

The myth of the necessity of patents during pandemics

The first myth is common: "If patent protection had not been available, [basic molecular] technologies, without which the vaccines could not have been made available in such a short time, might not have been developed in the first place"[6].

An investigation into the development of the vaccines tells a different story[2]. The work on mRNA vaccine technology dates back many decades and was almost entirely publicly funded[7,8]. Even some of the critical elements of the Pfizer–BioNTech and Moderna vaccines, such as the lipid nanoparticle container[5], were also publicly funded[7]. Both BioNTech and Moderna developed their own proprietary platforms — requiring considerable ingenuity, effort and cost — relying on both patents, trade secrets and regulatory exclusivity.

Pfizer's development of Paxlovid was conducted in-house. During the 2003 severe acute respiratory syndrome (SARS) outbreak, Pfizer developed an intravenous protease inhibitor to combat that coronavirus. Pfizer was able to do so as it had recently acquired Agouron Pharmaceuticals, a firm that had been working on a similar protease in rhinovirus[9]. Before Pfizer was able to test the molecule — PF-00835231 — in humans, the SARS outbreak ended and Pfizer shelved it[10]. For COVID-19, Pfizer dusted off PF-00835231 and did a significant amount of creative chemistry to change some of the features that prevented the drug from being taken orally. The resulting new molecule — PF-07321332 — constituted half of what became Paxlovid, the other half being ritonavir, which prevents the new molecule from being broken down[10]. Pfizer had applied for patents related to PF-00835231 but never pursued them[11–14]. The company was able to develop Paxlovid on its prior work and corporate know-how rather than on any patent[15].

While Pfizer, Moderna and other companies filed patents over their vaccines and antivirals, these provided a relatively minor incentive given other, more powerful, incentives. These incentives included both upfront grants to the companies and procurement contracts. According to its financial filings, Moderna received US$1.7 billion from the US government[16] while BioNTech received €375 million from the German government[17] and an additional €100 million from the European Commission to develop their vaccines[18]. The real pull for development came, however, from the mammoth procurement contracts issued by governments, entered well before any patents were issued[19]. While procurement contracts paid out only if the research was successful, the same is true for patents. As a result, Pfizer gained revenues of US$36.7 billion in 2021 from vaccine sales and expects another US$32 billion in 2022 for its vaccine and US$22 billion from Paxlovid; Moderna had revenues of US$17.7 billion in 2021 and is expecting sales of US$19 billion in 2022 (ref. [20]).

The Oxford–AstraZeneca vaccine was designed to be sold at cost. Oxford researchers had been investigating a vaccine against another coronavirus responsible for Middle East Respiratory Syndrome (MERS) when COVID-19 hit[21]. They shifted their efforts to SARS-CoV-2 in early 2020, funded almost entirely by government and philanthropy[22] and quickly developed a vaccine. They patented the vaccine and licensed it to AstraZeneca on the understanding that it would be broadly licensed and sold at cost during the pandemic[23]. The vaccine is available in more countries than any other[24].

Corbevax is an unpatented vaccine that has been transferred to companies in lower-income countries. Developed at Texas Children's Hospital and Baylor College of Medicine without government or industry support, the vaccine cost only US$7 million to develop[25,26] and some studies suggest it is approximately as effective as mRNA vaccines[27,28]. The developers of the vaccine transfer know-how to companies interested in manufacturing it, with those manufacturers responsible for seeking regulatory approval. Given the low cost, lack of complex cold chains and existing facilities in many developing countries, those manufacturers are located in those countries[29]. As a result, the vaccine is only licensed in developing countries.

Ultimately, it was not IP that played a significant role in vaccine development but rather government and philanthropic direct funding and, more significantly, procurement contracts. Patents appear to take on a more significant role once the first vaccines and antivirals have made it to market. For example, companies are vying to develop new lipid nanoparticles that better deliver mRNA to cells, have reduced side effects, and can be stored at higher temperatures[30].

The myth of access during a pandemic

While the first myth exaggerates the positive role that patents played in developing vaccines and antivirals, the second claims that the IP — a combination of patents, know-how and regulatory exclusivity — does not impair global access to vaccines

and antivirals[31]. An extreme view by a prominent IP scholar went so far as to say that: "There is no evidence that patents are undermining the creation and distribution of COVID-19 treatments. Indeed, the evidence all points to the opposite conclusion"[32].

Both the milder and extreme statements are wrong. Different vaccine and drug companies exercised their patents and trade secrets to control knowledge flows and threaten independent organizations — such as the World Health Organization's South African hub — from developing them, thus delaying access.

Moderna's CEO, Stéphane Bancel, understood that patents were not a major factor in maintaining the company's exclusivity in the market[33]. Thus, Moderna pledged to not enforce its patents related to its COVID vaccine in, or for sale in, low- and lower-middle-income countries[34]. Instead, Moderna relies on its secret know-how, refusing to share knowledge on how to construct an mRNA vaccine, even with the World Health Organization's South African hub, delaying development of an mRNA vaccine by the hub[35].

Further, the vaccine manufacturers are not the only companies holding IP. The developers of the lipid nanoparticle delivery system for mRNA vaccines hold a number of patents that are not widely licensed[7]. The existence of these patents — and the litigious nature of their holders — undermine the value of Moderna's non-enforcement pledge.

Pfizer holds onto its patents more tightly and, similar to Moderna, does not share know-how. An investigation found that a foundation representing Pfizer's partner, BioNTech, has threatened a World Health Organization vaccine hub in Africa with patent infringement[36].

Pfizer controls its vaccine-related patents through limited licensing arrangements[37]. One important exception is Pfizer's decision to license its Paxlovid patents through the Medicines Patent Pool to manufacture and sell Paxlovid in or for low- and lower-middle-income countries (and a limited number of upper-middle-income countries)[38,39]. Outside of the selected countries, Pfizer is limiting supplies of generic alternatives, as in Latin America[40]. This license leaves many vulnerable upper-middle-income countries without the ability to manufacture and distribute Paxlovid[41], a particular problem given the drug's low availability around the world[42]. Instead, Pfizer engages in charitable pricing of its vaccines and drugs in middle- and low-income countries[43,44]. The largest slice of its vaccine deliveries is through Covax, which has resulted in slow and insufficient global access[45–47].

As Peter Singer of the World Health Organization noted: "Charity is good, but we can't rely on charity alone"[48]. While offering lower prices two years into the pandemic was a step forward, charity does not address the essential problem of access: a steady and affordable supply of vaccines and antivirals. The first two years of the pandemic illustrated the limitations of this approach: prioritization of supply to high-income countries, vaccine nationalism and supply-chain issues, especially given the severe cold-chain requirements of mRNA vaccines. Instead, the World Health Organization and international experts call for manufacturing facilities either domestically or nearby to ensure access[48–50].

Certainly, efforts by Pfizer[51] and Moderna[52] to build manufacturing facilities in Africa are a step forward. But these facilities will take time to build, whereas both the Oxford–AstraZeneca and Corbevax vaccines have already led to manufacturing in lower-income countries around the world. Based on existing technology platforms, they enhance local capacity and supply chains[26] and thus offer a mechanism to ensure longer-term vaccine equity[5].

Beyond restraining access to the patents and know-how needed to manufacture vaccines and antivirals, Pfizer is resisting low- and middle-income country efforts to adapt Paxlovid to local health needs. For example, the Drugs for Neglected Diseases initiative reported that Pfizer blocked research on the feasibility of widening the treatment window for Paxlovid from five days to at least seven days to take into the account limitations in local health systems[53]. The company is also blocking combination trials aimed at delaying resistance to Paxlovid[54], a critical issue in the medium to long term.

Discussion

Once one puts aside the above myths that inform IP policy debates, one can more clearly see a path forward to both innovation and global equity in pandemic times. Here, I outline three positive steps that governments can take.

The first is that — as extraordinary as the development and testing of Paxlovid was — the world might have had antivirals much sooner had we globally adopted a different approach to drug development, one that is proactive rather than reactive. It was a stroke of luck that Pfizer had the PF-00835231 ready for development. One should not count on that luck being repeated next time.

Rather than rely on IP — patents and trade secrets — to supply us with antivirals after a pandemic hits, together, governments, researchers and companies can develop drugs in advance. We already know the viruses that will likely cause the next pandemic and we understand which targets are the most promising: polymerases and proteases[55]. Through open-science public–private partnerships — leveraging investments by governments, universities, the private sector and philanthropy — we already have the tools to proactively develop antivirals and take them up to Phase 1 trials in anticipation of the next health crisis. While no single company would have an incentive — given the risks — to develop antivirals in advance of a pandemic, the savings to governments of doing so are enormous and so the investment is worthwhile[1].

The second step is to realize that the almost exclusive reliance on the pull of IP on the private sector in order to bring vaccines and drugs forward is mistaken. More and better funded public efforts — such as Oxford–AstraZeneca and Corbevax — would broaden the paths to the successful development of vaccines and antivirals beyond those brought forward by firms relying mainly on IP.

The third step is for governments to insist that companies follow existing policies that require broad licensing of IP to speed development. For example, the Organisation for Economic Co-operation and Development (OECD) Council adopted Recommendations on the Licensing of Genetic Inventions in 2006 (ref. [56]) that promote broad licensing of foundational genetic technologies, including those involved with the mRNA vaccines: the mRNA sequences, the lipid nanoparticles and related processes. Companies failed to follow these recommendations and governments failed to push for compliance. If patent holders of the lipid nanoparticles had broadly licensed their technology[4] in accordance with the OECD recommendations, Afrigen Biologics would have been able to accelerate development of its mRNA vaccine for the World Health Organization hub[57].

Conclusions

During the pandemic, IP played a supporting, not a primary, role in developing vaccines and drugs. Myths concerning the role of IP get in the way of a holistic assessment of what IP can and cannot do, delaying or preventing the type of policy experimentation — such as open-science drug development — that promises to deliver more targeted vaccines and drugs to the world more quickly. ❐

E. Richard Gold
McGill University, Montreal, QC, Canada.
✉*e-mail: richard.gold2@mcgill.ca*

Published online: 7 October 2022
https://doi.org/10.1038/s41587-022-01485-x

References

1. Gold, E. R. & Edwards, A. M. *Front. Drug Discov.* **2**, 898654 (2022).
2. Sherkow, J. S., Ouellette, L. L., Nicholson, P. & Sachs, R. Are patents the cause of—or solution to—COVID-19 vaccine innovation problems? (No!). *Written Description* (4 March 2021).
3. Ning, C. et al. *Int. J. Environ. Res. Public Health* **19**, 5267 (2022).
4. Herder, M. *Health Policy* **17**, 15–25 (2022).
5. Maxmen, A. *Nature* **607**, 226–233 (2022).
6. Hilty, R. et al. *SSRN Electron. J.* https://doi.org/10.2139/ssrn.3841549 (2021).
7. Dolgin, E. *Nature* **597**, 318–324 (2021).
8. Lalani, H. S., Avorn, J. & Kesselheim, A. S. *Clin. Pharmacol. Ther.* **111**, 542–544 (2022).
9. Matthews, D. A. et al. *In Vitro Antiviral Activity of Human Rhinovirus 3C Protease Inhibitors Against the SARS Coronavirus.* (National Academies Press, 2004).
10. Halford, B. *ACS Cent. Sci.* **8**, 405–407 (2022).
11. Hoffman, R. L. et al. Anticoronaviral compounds and compositions, their pharmaceutical uses and materials for their synthesis (2005); https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2005113580
12. Kania, R. S., Mitchell, L. J. J. & Nieman, J. A. Anticoronaviral compounds and compositions, their pharmaceutical uses and materials for their synthesis. WIPO patent WO2006061714A3 (2005).
13. Fuhrman, S. A., Matthews, D. A., Patick, A. K. & Rejto, P. A. Inhibitors of SARS related coronavirus proteinase. WIPO patent WO2004093860A1 (2004).
14. He, M., Kania, R.S., Lou, J. & Planken, S. Inhibitors of SARS 3C like protease. US patent US20060014821A1 (2004).
15. Matthews, D. A. Development of Paxlovid. *Chemical & Engineering News* (March 7, 2022).
16. Wilkerson, J. Govt. pays Moderna $308M for pediatric studies of COVID-19 vaccine. *Inside Health Policy* (12 May 2022).
17. BioNTech to receive up to €375M in funding from German Federal Ministry of Education and Research to support COVID-19 vaccine program BNT162. *BioNTech* (15 September 2020).
18. *EU Research and Innovation Supporting Vaccine Development for COVID-19* (Publications Office of the EU, 2021).
19. Dale, D. Fact-checking the battle for credit over Pfizer's vaccine announcement. *CBS58* (10 November 2020).
20. Kimball, S. What's next for Pfizer, Moderna beyond their projected $51 billion in combined Covid vaccine sales this year. *CNBC* (3 March 2022).
21. The story behind the Oxford-AstraZeneca COVID-19 vaccine success. *UKRI* (30 November 2021).
22. Cross, S. et al. *BMJ Glob. Health* **6**, e007321 (2021).
23. Hancock, J. Rather than give away its COVID vaccine, Oxford makes deal with drugmaker. *WUSF Public Media* (25 August 2020).
24. Holder, J. Tracking coronavirus vaccinations around the world. *The New York Times* (15 August 2021).
25. Texas Children's Hospital and Baylor College of Medicine Covid-19 vaccine technology secures emergency use authorization in India. *Texas Children's Hospital* (28 December 2021).
26. Ferran, M. Corbevax, a new patent-free COVID-19 vaccine, could be a pandemic game changer globally. *The Conversation* (19 January 2022).
27. Thuluva, S. et al. Preprint at *medRxiv* https://doi.org/10.1101/2022.03.20.22271891 (2022).
28. Thuluva, S. et al. Preprint at *medRxiv* https://doi.org/10.1101/2022.03.08.22271822 (2022).
29. Holmes, B. Should traditional vaccines be used in the global fight against Covid? *Smithsonian Magazine* (22 April 2022).
30. Dolgin, E. *Science* **376**, 680–681 (2022).
31. McMurry-Heath, M. Waiving intellectual property rights would compromise global vaccination efforts. *Stat* (18 August 2021).
32. Mossoff, A. *Pandemics, Patents, and Price Controls* (The Heritage Foundation, 2021).
33. Asgari, N. & Kuchler, H. Moderna CEO 'didn't lose sleep' over US backing of patent waiver. *Financial Times* (6 May 2021).
34. Moderna announces its global public health strategy. *Moderna Inc.* (7 March 2022).
35. Kumar, A. Afrigen: a step toward Africa's first Covid-19 vaccine of its own. *Inter Press Serv.* (16 February 2022).
36. Davies, M. *Br. Med. J.* **376**, o304 (2022).
37. Wise, J. *Br. Med. J.* **377**, o1086 (2022).
38. Pfizer and The Medicines Patent Pool (MPP) sign licensing agreement for COVID-19 oral antiviral treatment candidate to expand access in low- and middle-income countries. *Pfizer* (16 November 2021).
39. *Nirmatrelvir* (Medicines Patent Pool, 2021).
40. Stolberg, S. G. As poor nations seek Covid pills, officials fear repeat of AIDS crisis. *The New York Times* (8 May 2022).
41. MSF response to license between Pfizer and Medicines Patent Pool for new COVID-19 treatment Paxlovid. *Medicins sans Frontières* (16 November 2021).
42. Green, A. & Paun, C. The battle for Paxlovid. *Politico* (19 May 2022).
43. *Working to Reach Everyone, Everywhere* (Pfizer, accessed 6 September 2022); https://www.pfizer.com/science/coronavirus/vaccine/working-to-reach-everyone-everywhere#
44. Pfizer launches 'an accord for a healthier world' to improve health equity for 1.2 billion people living in 45 lower-income countries. *Pfizer* (25 May 2022).
45. Covid vaccines: How fast is progress around the world? *BBC News* (1 June 2022).
46. de Bengy Puyvallée, A. & Storeng, K. T. *Global. Health* **18**, 26 (2022).
47. Feinmann, J. *Br. Med. J.* **374**, (2021).
48. Maxmen, A. *Nature* **597**, 455–457 (2021).
49. Sirleaf, E. J. & Clark, H. *Transforming or Tinkering? Inaction Lays the Groundwork for Another Pandemic* (Independent Panel for Pandemic Preparedness and Response, 2022).
50. Zaidi, A. Geographically distributed manufacturing capacity is needed for improved global health security. *Bill & Melinda Gates Foundation* (28 July 2021).
51. Khemlani, A. Pfizer's South Africa vaccine partnership won't impact global vaccination goals. *Yahoo Finance* (4 March 2022).
52. Moderna to build mRNA vaccine manufacturing facility in Kenya. *Reuters* (7 March 2022).
53. Pfizer blocking research to generate evidence on optimal use of novel antiviral for COVID-19 patients in low- and middle-income countries. *DNDi* (15 March 2022).
54. Langreth, B., Muller, M. & Griffin, R. Pfizer's tight Paxlovid rein stymies drug combination research. *BNN Bloomberg* (18 May 2022).
55. Edwards, A. M., Baric, R. S., Saphire, E. O. & Ulmer, J. B. *Science* **375**, 1133–1139 (2022).
56. *Recommendation of the Council on the Licensing of Genetic Inventions* (OECD, 2022).
57. Maxmen, A. *Nature* **602**, 372–373 (2022).

Competing interests

The author declares no competing interests.