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Addressing Exclusivity Issues: COVID-19 and Beyond

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I INTRODUCTION

Almost every aspect of the COVID-19 response, from vaccines, diagnostics, and therapeutics to medical equipment, tracking systems, software, and other innovations, are or will become subject to some form of exclusive rights.[1] Many of these involve intellectual property rights (IPRs).[2] By offering innovators the exclusive right to exploit their innovations while recouping research and development (R&D) costs and other expenditures, IPRs may incentivize the development of new technologies.[3] But IPRs may also preclude others from important research, manufacturing, and distribution.[4] In the same vein, these exclusionary rights allow right holders to set prices in the absence of competition. Since this may limit access to innovations that are crucial for tackling pandemics, IPRs are a key factor in pandemic response and preparedness.

Consequently, IPRs have generated much controversy around the globe. Many of these debates have focused on traditional IPRs, particularly patent rights. Numerous existing patent claims cover new chemical or molecular entities. Patents are also filed for repurposed drugs and vaccine platforms (e.g., COVID-19 mRNA platforms), with separate patent protection for the vaccine and its elements, including viral particles, adjuvants, and vaccine boosters. Even in situations where no patent

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[1] Frank Tietze et al., Crisis-Critical Intellectual Property: Findings From the COVID-19 Pandemic, Inst. of Elec. & Elecs. Eng'rs Transactions Eng'g Mgmt. (2020), https://ieeexplore.ieee.org/stamp/stamp.jsp?tp=&arnumber=9120047; see also Cynthia Liu et al., Research and Development on Therapeutic Agents and Vaccines for COVID-19 and Related Human Coronavirus Diseases, 6 ACS *Central Sci.* 315 (2020); Sven J.R. Bostyn, Access to Therapeutics and Vaccines in Times of Health Pandemics: How Exclusivity Rights Can Affect Such Access and What We Can Do About It, 2020 Intell. Prop. Q. 227-70 (2020).

[2] Intellectual property rights include patents, copyrights, and similar forms of legal protection, such as trade secrets.

[3] Jorge L. Contreras et al., Pledging Intellectual Property for COVID-19, 38 *Nat. Biotechnol.* 1146 (2020).

[4] Id.

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protection is available, many COVID-19 therapeutics and vaccines will also obtain regulatory, data, and market exclusivities.

Consequently, the design and application of regulatory exclusivities have become increasingly important in general innovation policy debates.[5] This chapter addresses exclusivity issues, with a particular emphasis on regulatory exclusivities for vaccines and therapeutics. We begin with a basic overview of the current regulatory exclusivity landscape in Europe and the United States, followed by a discussion of current developments in COVID-19 vaccines and therapeutics. Next, we describe the influence of these technological developments on debates surrounding regulatory exclusivities while describing their relationship to other forms of exclusivities. From these assessments, we draw some lessons for market exclusivity, innovation, and access during the COVID-19 pandemic and beyond.

II CURRENT REGULATORY EXCLUSIVITY LANDSCAPE

A *Two Forms of Exclusivity*

Two forms of exclusivity are particularly relevant to the treatment and prevention of pandemics: patent and regulatory. In the European and US systems of regulatory exclusivity, data and marketing exclusivities do not depend on patents but are often cumulative with patent protection.[6]

1 Europe

Patents in Europe last twenty years from the date of filing. Patent-like protection can be sustained beyond twenty years by a Supplementary Protection Certificate (SPC),[7] which compensates for regulatory approval procedures by adding a maximum of five years to the patent term. Six additional months of SPC extension can be obtained for conducting studies in compliance with a pediatric investigation plan.[8] SPCs apply only to patent-protected products and cannot be added to regulatory exclusivities.

European legislation also offers patent-independent regulatory exclusivity under the 8+2+1 principle for both small molecule drugs and biologics such as vaccines.[9]

[5] See, generally, Timo Minssen, Assessing the Inventiveness of Bio-Pharmaceuticals under European and US Patent Law at 7, 315, 321, 323–24 (Nov. 16, 2012) (Ph.D. dissertation, Lund University Faculty of Law) (on file with author).

[6] Sven J.R. Bostyn et al., Effects of Supplementary Protection Mechanisms for Pharmaceutical Products, Technopolis Grp. 61, 61–73 (May 2018), www.technopolis-group.com/report/effects-of-supplementary-protection-mechanisms-for-pharmaceutical-products/; see also Directive 2001/83, of the European Parliament and of the Council of Nov. 6, 2001 on the Community Code Relating to Medicinal Products for Human Use, art. 10(1) (hereinafter, Directive 2001/83/EC).

[7] Council Regulation 469/2009 of May 6, 2009, Supplementary Protection Certificates for Medicinal Products.

[8] Id. at art. 13(3); see also Bostyn et al., supra note 6, at 30–60.

[9] Directive 2001/83/EC, supra note 6.

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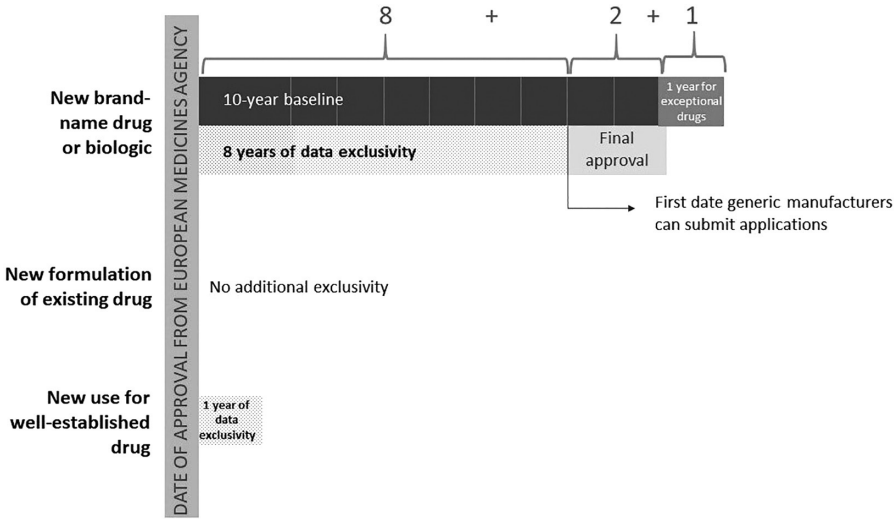

FIGURE 16.1 MA process in Europe

Once approved, a drug obtains automatic data protection for eight years, provided it is the first marketing authorization (MA) for that active ingredient in Europe. During this period, no third party can refer to the data in the regulatory dossier of the reference medicinal product, including competitors seeking to file an abridged generic application. An approved drug also receives ten years of marketing exclusivity starting from the date of approval, protecting the reference product against market entry by third parties during the term. There are also three options for obtaining one additional year of exclusivity.[10] The various types of exclusivities available in Europe are illustrated in Figure 16.1.

This Global Marketing Authorization is issued only once for a given drug product and cannot be renewed or extended for any additional strengths, forms, routes of administration, or presentations, or for any future variations and extensions.[11] Subsets of genetic profiles requiring specific treatment for COVID-19 might lead to the development of drugs for which orphan designation and MA can be obtained.[12]

In Europe, there are three main categories for obtaining an MA: central, decentralized, and mutual recognition procedure. For biologics, including vaccines, and new

[10] Id. One additional year of marketing exclusivity may be granted for new therapeutic indications showing significant clinical benefit in comparison with existing therapies (art. 10(1), para. 4); one year of data protection for new indications of well-established substances (art. 10(5)); and one year of protection for data supporting a change of classification (e.g., from prescription drug to over-the-counter) (art 74a). These additional terms of exclusivity are not cumulative, so the total duration of protection cannot exceed eleven years.

[11] Id., art. 6(1), para 2; see also Bostyn et al., supra note 6, at 65.

[12] Ten years of marketing exclusivity is awarded for orphan drugs; see Council Regulation 141/2000 of Dec. 16, 1999, Orphan Medicinal Products, art. 8.

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small molecules for viral diseases, the central procedure at the European Medicines Agency (EMA) must be followed.[13] For new indications for already existing small molecules, the decentralized and mutual recognition procedure can be followed.

The main categories of MAs are full and conditional.[14] To date, COVID-19 vaccines and therapeutics have all been issued conditional MAs, which are applied to products aimed at treating, preventing, or diagnosing seriously debilitating or life-threatening diseases. Other medicinal products falling within the scope of the regulations are orphan drugs and medicinal products to be used in emergency situations, in response to public health threats recognized either by the World Health Organization (WHO) or by the European Community in the framework of Decision No. 2119/98/EC.[15]

Conditional MAs may be granted in emergency situations if the EMA Committee for Medicinal Products for Human Use finds that all the following requirements are met: (1) the benefit–risk balance of the product is positive; (2) it is likely that the applicant will be able to provide comprehensive data; (3) unmet medical needs will be fulfilled; and (4) the benefit to public health of the medicinal product's immediate availability on the market outweighs the risks due to need for further data.[16]

2 United States

In the United States, the Patent Act, the Hatch-Waxman Act, and related legislation defines marketing exclusivity periods for pharmaceuticals and biologics.[17] Patent protection for pharmaceutical products in the United States is comparable to that of Europe: twenty years of patent protection, with a patent term restoration period of up to five years for time spent during the regulatory process, and a pediatric exclusivity period of six months for certain drugs studied in pediatric populations pursuant to a written request.[18]

Regulatory exclusivity for new drug application (NDA) applicants exists as a five-year New Chemical Entity exclusivity, a three-year new clinical investigation exclusivity, a seven-year orphan drug exclusivity under the Orphan Drug Act,

[13] Council Regulation 726/2004 of Mar. 31, 2004, Community Procedures for the Authorization and Supervision of Medicinal Products for Human and Veterinary Use and Establishing a European Medicines Agency, art. 3(1), annex.

[14] Commission Regulation No 507/2006 of Mar. 29, 2006, Conditional Marketing Authorization for Medicinal Products for Human Use Falling within the Scope of Regulation (EC) No. 726/2004 of the European Parliament and of the Council.

[15] Id., art. 2.

[16] Id., art. 4.

[17] Aaron S. Kesselheim, Michael S. Sinha & Jerry Avorn, Determinants of Market Exclusivity for Prescription Drugs in the United States, 177 *JAMA Intern. Med.* 1658, 1658 (2017).

[18] Id.; see also Michael S. Sinha et al., Labeling Changes and Costs for Clinical Trials Performed Under the US Food and Drug Administration Pediatric Exclusivity Extension, 2007 to 2012, 178 *JAMA Intern. Med.* 1458, 1458 (2018).

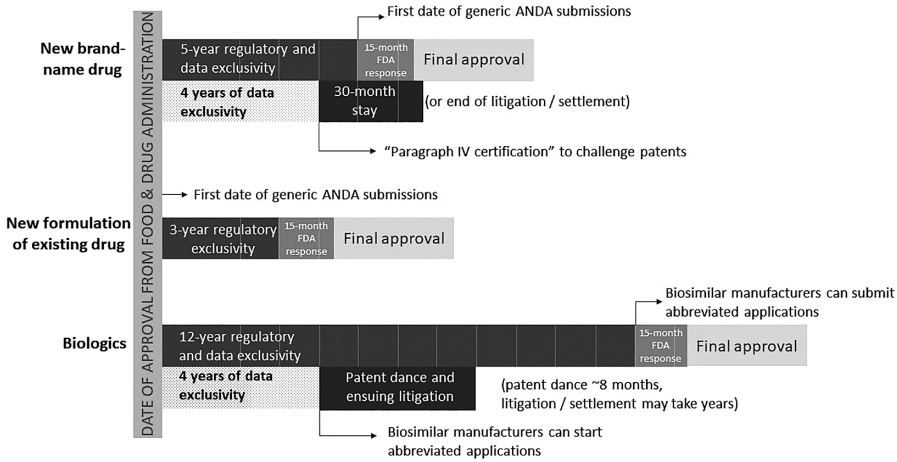

FIGURE 16.2 MA process in the United States

or a twelve-year biologic exclusivity under the Biologics Price Competition and Innovation Act.[19] There is no comparable process of conditional approval.

For new chemical entities, data exclusivity extends for five years as well, though generic manufacturers can begin utilizing originator data after four years for the preparation of generic drug applications. Unlike in Europe, the United States does offer three-year periods of exclusivity for new formulations of existing drugs, though no data exclusivity applies. For biologics, data exclusivity protections run for twelve years, but biosimilar manufacturers can begin using data after the fourth year to develop competing products.[20] Review time by the FDA for generic products is approximately fifteen months. Drugs and vaccines for COVID-19 were evaluated through a relatively new regulatory process known as Emergency Use Authorization (EUA).

EUAs are a byproduct of several post-9/11 laws, including the Project Bioshield Act of 2004 and the Pandemic and All-Hazards Preparedness Act of 2013. When invoked during a public health emergency such as COVID-19, an EUA permits broad use of unlicensed products as long as the benefits outweigh risks.[21] The particulars of available regulatory exclusivities under US law are illustrated in Figure 16.2.

[19] Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended in scattered sections of 21 U.S.C.); Orphan Drug Act of 1983, Pub L. No. 97-414, 96 Stat. 2049 (codified as amended in scattered sections of 21 U.S.C., 26 U.S.C., and 42 U.S.C.); Patient Protection and Affordable Care Act, Pub. L. No. 111-148, 124 Stat. 119 (2010) (codified as amended in scattered sections of 26 U.S.C. and 42 U.S.C.).

[20] See Timo Minssen & Justin Pierce, Big Data and Intellectual Property Rights in the Health and Life Sciences, in Big Data, Health Law, and Bioethics 311 (I. Glenn Cohen et al., eds., 1st ed. 2018).

[21] See Food & Drug Admin., Guidance Document: Emergency Use Authorization of Medical Products and Related Authorities (Jan. 2017), www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities.

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B *COVID-19 Vaccines*

Pandemics create a time pressure to develop vaccines as quickly as possible, which concentrates the cost of development over a very short time window. Given the crippling effects of pandemics on the economy and health care systems, governments are often extremely willing to commit capital to accelerate vaccine development. Government funding will typically be in the form of push incentives (e.g., funding R&D in developing new vaccines) and pull incentives (e.g., in the form of advance purchase agreements or other advance market commitments).[22] Yet the exclusive rights structure after regulatory clearance or approval remains unchanged, and final vaccines are fully owned by pharmaceutical companies, even those developed with significant government funding and collaboration.

In Europe, the European Commission joined forces with several countries to collect research funding under the Coronavirus Global Response, which strives for "universal access to affordable coronavirus vaccination, treatment[,] and testing,"[23] as part of the WHO's global call for action.[24] In the United States, investment in vaccine development largely occurred through a federal initiative known as Operation Warp Speed, though execution was largely in conjunction with federal agencies such as the National Institutes of Health. Agencies within the Department of Defense, including the Biomedical Advanced Research and Development Authority and the Defense Advanced Research Projects Agency, have historically been involved in vaccine development as well; the former agency contributed nearly $6 billion each to the Pfizer and Moderna COVID-19 mRNA vaccines.[25]

Vaccine R&D over the last few decades has largely occurred within small and medium-sized companies.[26] Therefore, pushing vaccine candidates through clinical trials and scaling up production is often dependent on additional federal funding or acquisition by larger firms; between 1990 and 2012, small and medium-sized

[22] Rachel Sachs, Lisa Larrimore Ouellette, W. Nicholson Price II & Jacob S. Sherkow, Innovation Law and COVID-19: Promoting Incentives and Access for New Health Case Technologies (Chapter 15 in this book).

[23] Participating countries include Canada, France, Germany, Italy, Japan, Saudi Arabia, Norway, Spain, and the United Kingdom. The United States declined to participate.

[24] See World Health Org., Coronavirus Global Response (2020), https://global-response.europa.eu/index_en. Around €16 billion have been pledged, with €15 billion coming from EU member states. Funding recipients include the Coalition for Epidemic Preparedness Innovation, for vaccines; Gavi, the Vaccine Alliance, for vaccine deployment (related to coronavirus); Therapeutics Accelerator, for therapeutics; UNITAID, for therapeutics deployment; the Foundation for Innovative New Diagnostics, for diagnostics; the Global Fund, for diagnostics deployment; and the WHO, for health systems.

[25] Michael S. Sinha et al., Expansion of the Priority Review Voucher Program under the 21st Century Cures Act: Implications for Innovation and Public Health, 44 *Am. J. Law Med.* 329, 329 (2018); see also US Cong. Budget Off., Research and Development in the Pharmaceutical Industry (Apr. 2021), www.cbo.gov/file-download/download/private/161984.

[26] Thomas J. Hwang & Aaron S. Kesselheim, Vaccine Pipeline Has Grown During The Past Two Decades With More Early-Stage Trials From Small And Medium-Size Companies, 35 *Health Affs. (Millwood)* 219, 219 (2016).

companies accounted for 71 percent of Phase I vaccine trials but only 38 percent of Phase III trials.[27] Many products will languish if funding runs dry or large vaccine manufacturers decline to conduct further studies or pursue an MA. For emerging infectious diseases, this has historically been termed the "valley of death." Even with an urgent push to develop a vaccine – as was the case with the Ebola epidemic – waning interest in the face of a geographically limited outbreak can result in the shelving of important projects prior to clinical testing and approval.[28]

To date, this has not been the story of COVID-19 vaccines. Global R&D efforts and advance market commitments have yielded several promising vaccines, but the issue of exclusive rights has unfortunately been pushed aside. Apart from the fact that the vaccine itself is subject to patent protection and/or regulatory exclusivities, many of the COVID-19 vaccines are based on proprietary platforms. Moderna has a large patent portfolio covering their mRNA vaccine platform, boasting on its website that it "has been granted over 100 patents in the [United States], Europe, Japan[,] and other jurisdictions, protecting fundamental inventions in the mRNA therapeutics space, with several hundred additional pending patent applications covering key advances in the field."[29] Similar patent libraries protect the Pfizer/BioNTech and CureVac mRNA platforms, to the extent that "Moderna, CureVac, BioNTech[,] and GSK collectively own nearly half of the mRNA vaccine patent applications."[30] Trade secrets will also play an important role when it comes to vaccine manufacturing methods.[31] See Table 16.1 for more about COVID-19 vaccines in use and in development.

Focusing on regulatory exclusivities, we can discern different dynamics in Europe and the United States. All vaccines, as new biological products, will be able to benefit from regulatory exclusivities. In Europe, all vaccines approved have received conditional market approval; the regulatory exclusivity period of 8+2 years starts running immediately. In the United States, the vaccines that have currently received an EUA follow a different regulatory path.[32] A Biologics Licensing Application (BLA) would secure permanent regulatory approval of the vaccine by the FDA, but EUAs are temporary and typically expire once the public health emergency ends.[33]

[27] Id.

[28] Denise Grady, Ebola Vaccine, Ready for Test, Sat on the Shelf, NY Times (Oct. 23, 2014), www.nytimes.com/2014/10/24/health/without-lucrative-market-potential-ebola-vaccine-was-shelved-for-years.html.

[29] Moderna's Intellectual Property, www.modernatx.com/mrna-technology/modernas-intellectual-property.

[30] See Cecilia Martin & Drew Lowery, mRNA Vaccines: Intellectual Property Landscape, 19 *Nature Rev. Drug Disc.* 578, 578 (2020).

[31] W. Nicholson Price II & Arti K. Rai, How Logically Impossible Patents Block Biosimilars, 37 *Nat. Biotechnol.* 862, 862 (2019).

[32] US Food & Drug Admin., COVID-19 Vaccines, www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines.

[33] See Food & Drug Admin., supra note 21.

TABLE 16.1 *Regulatory status and launch prices of COVID-19 vaccines*[34]

Manufacturer	Product Name	Product Type	Dosing Regimen	Approval Status (EU)	Launch Price per Dose (EU)	Approval Status (US)	Launch Price per Dose (US)
Pfizer/ BioNTech	Comirnaty	mRNA (modified nucleoside)	2 doses 3 weeks apart	Conditional approval 12/21/2020	€12	Full approval 8/23/2021	$19.50
Moderna	Spikevax	mRNA (modified nucleoside)	2 doses 4 weeks apart	Conditional approval 1/6/2021	€15	Full approval 1/31/2022	$15
Oxford/ AstraZeneca	Vaxzevria/ Covishield	Viral vector	2 doses 4 to 12 weeks apart	Conditional approval 1/29/2021	£1.61	To be determined	$3–4
J&J/Janssen	Janssen COVID-19 Vaccine	Viral vector	1 dose	Conditional approval 3/11/2021	£6.30	EUA 2/27/2021	$10
Novavax	NVX- CoV2373	Protein subunit	2 doses 3 weeks apart	Conditional approval 12/20/2021	€17.80	EUA 7/13/2022	$16
Sanofi/GSK					€7.56	To be determined	$10.50

[34] EU Prices: Sarah Boseley, Belgian Minister Tweets EUs COVID Vaccine Price List to Anger of Manufacturers, Guardian (Dec. 18, 2020), www.theguardian.com/world/2020/dec/18/belgian-minister-accidentally-tweets-eus-covid-vaccine-price-list; US Prices: Owen Dyer, COVID-19: Countries are Learning What Others Paid for Vaccines, 372 *Brit. Med. J.* n.281 (2021); see also C. Buddy Creech et al., SARS-CoV-2 Vaccines, 325 *J. Am. Med. Ass'n.* 1318, 1319 (2021) (data updated as of July 20, 2022).

Importantly, EUAs do not trigger the beginning of regulatory exclusivity windows, meaning that the Moderna and Pfizer vaccines, which have been distributed to hundreds of millions of Americans, received their full twelve-year marketing and data exclusivity periods only after BLA approval. When it developed statutory provisions granting regulatory exclusivity, Congress likely did not anticipate a scenario in which millions of vaccines could be distributed, and billions of dollars in revenues earned, without triggering regulatory exclusivity periods.

The director of the FDA's Center for Biologics Evaluation and Research, Dr. Peter Marks, described the EUA process as an "EUA-plus," noting that a vaccine EUA "is going to be closer" to full BLA approval.[35] The FDA's "EUA-plus" standard for vaccines seems more aligned with conditional approval in Europe, except that in Europe the clock has already started running on regulatory exclusivities.

With this in mind, vaccine manufacturers are arguably incentivized to delay full BLAs until the public health emergency ends and the EUA is not reauthorized. Indeed, EUAs for past infectious disease outbreaks have been renewed several times, with no guarantee of a later-filed full licensing application.[36]

C *COVID-19 Therapeutics*

Therapeutics are largely governed by the same rules as vaccines. Upon approval, new chemical entities receive full regulatory periods in both Europe and the United States, governed by the rules set out in Section II. A. In Europe, the clock begins at the time of conditional approval. In the United States, an EUA does not trigger the initiation of regulatory approval periods.

For new uses of existing drugs, regulatory exclusivities may apply even if no patent protection can be obtained. In Europe, options to gain additional regulatory exclusivity protection for repurposed drugs are quite limited. Repurposing could be patent protected in Europe as a so-called further medical indication patent,[37] but under the Global Marketing Authorization, with a few notable exceptions,[38] no renewal or extension of regulatory exclusivities is possible. In the United States, periods of guaranteed market exclusivity can be obtained regardless of patent status; this includes reformulated drug products, which may obtain NDAs or supplemental NDAs.

[35] Sarah Owermohle, Marks: Prepare for 'EUA-plus' for COVID Vaccines, Politico (Sept. 11, 2020), www.politico.com/newsletters/prescription-pulse/2020/09/11/marks-prepare-for-eua-plus-for-covid-vaccines-790343.

[36] US Food & Drug Admin., Emergency Use Authorization, www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.

[37] Convention on the Grant of European Patents, art. 54(5), Oct. 5, 1973, 1065 U.N.T.S. 199; see also Sven J.R. Bostyn, Personalised Medicine, Medical Indication Patents and Patent Infringement: Emergency Treatment Required, *Intell. Prop. Q.* 151, 155–58 (2016); Christopher M. Holman, Timo Minssen & Eric M. Solovy, Patentability Standards for Follow-On Pharmaceutical Innovation, 37 *Biotechnology Law Rep.* 131 (2018).

[38] Directive 2001/83/EC, art. 6(1), para. 2.

In the United States, Operation Warp Speed invested far more into COVID-19 vaccines as compared to therapeutics. Globally, the trend is similar: 95 percent of all investments have gone into vaccines, with only 5 percent devoted to therapeutics.[39] Some clinical trials have evaluated the efficacy of marketed antivirals in the fight against COVID-19.

In Europe, remdesivir (Veklury) was conditionally authorized by the EMA for the treatment of COVID-19; in the United States, remdesivir received full FDA approval. The WHO raised issues about remdesivir's efficacy, amending its guidelines accordingly,[40] but in Europe, the drug remains conditionally approved while the EMA continues to evaluate the data. Despite questions about its efficacy, remdesivir is FDA-approved in the United States and costs $3,120 for a five-day course of treatment when purchased by private insurers ($2,340 when purchased by public payers such as Medicare and Medicaid).[41] The drug is still under patent protection: its primary US patent will lapse in 2031 and in Europe in 2035. Other antivirals are being studied, including favipiravir, which is authorized in Japan for the treatment of influenza.[42] Merck recently reported that its antiviral drug molnupiravir "reduced the risk of admission to hospital or death by around 50 percent in non-hospitalized adults who had mild to moderate COVID-19 and were at risk of poor outcomes"; it has requested an EUA from the FDA.[43] Pfizer initiated clinical studies of PF-07321332, its investigational COVID-19 antiviral drug, in August 2021.[44] The drug, later named nirmatrelvir (Paxlovid), received an EUA in December 2021 and has since become a mainstay in COVID-19 treatment in the United States.[45]

The injectable corticosteroid dexamethasone, an older medication that has no patent or regulatory protection, showed considerable promise in treating COVID-19.[46] However, the lack of exclusivities for dexamethasone in the United States and Europe give pharmaceutical companies little incentive to rigorously study its use

[39] Governments Spent at Least €93bn on COVID-19 Vaccines and Therapeutics During the Last 11 Months, Bus. Wire (Jan. 11, 2021), www.businesswire.com/news/home/20210110005098/en/Governments-Spent-at-Least-%E2%82%AC93bn-on-COVID-19-Vaccines-and-Therapeutics-During-the-Last-11-Months.

[40] World Health Org., Therapeutics and COVID-19: Living Guideline (Mar. 31, 2021), www.who.int/publications/i/item/therapeutics-and-covid-19-living-guideline.

[41] Allison Inserro, Gilead Sciences sets US Price for COVID-19 Drug (June 29, 2020), www.ajmc.com/view/gilead-sciences-sets-us-price-for-covid19-drug-at-2340-to-3120-based-on-insurance.

[42] Glenmark Begins Phase III Trials of Favipiravir for COVID-19 in India, Clinical Trials Arena (May 13, 2020), www.clinicaltrialsarena.com/news/glenmark-favipiravir-trial-begins/.

[43] COVID-19: Molnupiravir Reduces Risk of Hospital Admission or Death by 50% in Patients at Risk, MSD Reports, 375 *Br. Med. J.* n.242 (2021).

[44] A Study of PF-07321332/Ritonavir in Non-Hospitalized Low-Risk Adult Participants With COVID-19, ClinicalTrials.gov, https://clinicaltrials.gov/ct2/show/NCT05011513.

[45] Spencer Kimball, Paxlovid Prescriptions to Treat COVID Increased Tenfold in U.S. Since Late February, Pfizer Says, CNBC (May 3, 2022), www.cnbc.com/2022/05/03/pfizer-paxlovid-prescriptions-to-treat-covid-increased-tenfold-in-us-since-late-february.html.

[46] RECOVERY Collaborative Group et al., Dexamethasone in Hospitalized Patients with COVID-19, 384 *N. Engl. J. Med.* 693 (2020).

in COVID-19. That said, a significant benefit of dexamethasone is its low cost, which is driven by the existence of multiple generic manufacturers for the product.[47]

Various antibody treatments have also been studied in clinical trials.[48] For instance, the Regeneron antibody cocktail contains human antibodies harvested from COVID-19 patients combined with mouse monoclonal antibodies against the spike protein.[49] Initially available in the United States only via compassionate use or participation in clinical trials, several monoclonal antibodies have since been granted EUAs.

III IMPACT OF REGULATORY EXCLUSIVITIES ON ACCESS TO COVID-19 MEDICAL TREATMENTS

The list of drug and vaccine candidates for COVID-19 that are authorized or in various stages of development is extensive; many are protected by patents or eligible for regulatory exclusivities. These exclusive rights allow manufacturers to determine access and price in the absence of suitable substitutes. COVID-19 vaccines have yet to compete on price because the manufacturers contract with the government for certain quantities of vaccine at fixed prices; those prices, in fact, have risen over time. Exclusive rights offer a significant incentive for the development of vaccines and therapeutics for COVID-19.

Even though the effects of exclusive rights on access are similar for therapeutics and vaccines, the situation is more complicated for vaccines, as there are more parameters to consider: vaccine platforms, vaccine adjuvants, the vaccines themselves, and the complex manufacturing processes for those vaccines, which are often shrouded in trade secrecy. The broadly patented vaccine platforms may slow the development of other vaccines as third parties, unable to make use of patented platforms, are either blocked from entering the market or require a costly licensing agreement. Early on, manufacturers declared their intent not to engage in price gouging,[50] meaning that prices would not rise during the "crisis" phase – presumably the duration of the public health emergency. Yet taxpayers have little information regarding the costs and conditions of vaccine purchasing agreements. The prices listed in Table 16.1 have already started to increase as manufacturers move away from "pandemic pricing" limits.[51] Indeed, Pfizer and Moderna have

[47] Id. at 702.

[48] See Bostyn, supra note 1, at 250–53.

[49] Johanna Hansen et al., Studies in Humanized Mice and Convalescent Humans Yield a SARS-CoV-2 Antibody Cocktail, 369 *Sci.* 1010 (2020).

[50] Andrew Dunn, The CEO of the Buzzy Biotech That's Working on a Potential Coronavirus Vaccine Just Pledged He Won't Set a High Price for the Shot, Bus. Insider (Mar. 4, 2020), www.businessinsider.com/moderna-ceo-stephane-bancel-interview-coronavirus-vaccine-price-2020-3.

[51] Deborah Abrams Kaplan & Peter Wehrwein, The Price Tags on the COVID-19 Vaccines, 31 *Managed Healthcare Exec.* 26 (2021) ("During an earnings call in early February, Pfizer CFO Frank D'Amelio described Pfizer's $19.50-per-dose price as 'pandemic pricing' and 'that's not a normal price like we typically get for a vaccine, $150, $175 per dose.'").

increased the prices of their vaccines, including for Omicron-adapted versions, in both Europe and the United States.[52] Though such price increases are good news for investors, they do not bode well for global access.[53]

The presence of extensive patent, regulatory exclusivities, and trade secrets also positions manufacturers in opposition to compelled licensing agreements. We see this already playing out with the shortage of supplies in vaccines. Unwillingness to license vaccine manufacturing to third parties – and limited leverage among payers to compel such licensing – makes patients very vulnerable to delays and disruptions in manufacturing, as we have seen with the AstraZeneca vaccine in Europe.[54]

Even though voluntary sharing of technology is always an option, there is little evidence this is happening for most COVID-19-related technology.[55] AstraZeneca has a licensing agreement in place with Serum Institute India to produce and distribute one billion doses of the AZ/Oxford COVID-19 vaccine;[56] a similar license is in place with Dutch company Halix BV.[57] For the other authorized vaccines, no production licensing agreements are in place. The Medicines Patent Pool, a United Nations-backed public health organization working to increase access to, and facilitate the development of, life-saving medicines for low- and middle-income countries,[58] has extended its mission to include COVID-19 products, but has yet to negotiate licensing agreements. Similarly, the WHO COVID-19 Technology Access Pool (C-TAP) has not led to sufficient sharing of technology or treatments. Though patents present a significant obstacle for technology sharing, their issuance depends on full disclosure and enablement; even if patented technology is licensed, institutional expertise held as trade secrets likely poses greater barriers to the sharing and scale-up of vaccine technology.[59]

[52] Fraiser Kansteiner, Pfizer, Moderna Hike COVID-19 Vaccine Prices in New European Supply Deals: Report, Fierce Pharma (Aug. 2, 2021), www.fiercepharma.com/pharma/pfizer-moderna-turn-up-covid-19-vaccine-prices-europe-as-companies-plot-deliveries-into-2022; Fraiser Kansteiner, Pfizer's Latest $3.2b Pandemic Vaccine Contract Suggests Private Market Still a Ways Off: Analysts (June 30, 2022), www.fiercepharma.com/pharma/pfizers-latest-32b-pandemic-vaccine-contract-suggests-private-market-still-ways-analysts ("[T]he U.S. has laid out $3.2 billion for another 105 million doses of Pfizer-BioNTech's mRNA shot Comirnaty[;] … [t]he deal breaks down to around $30.50 per dose.").

[53] Josh Nathan-Kazis, Pfizer Raises COVID Vaccine Price 27%. What It Means for the Stock, Barron's (June 30, 2022), www.barrons.com/articles/pfizer-stock-vaccine-price-increase-51656594199.

[54] Rob Davies, Why the EU and AstraZeneca Are Stuck in a COVID Vaccines Row, Guardian (Jan. 27, 2021), www.theguardian.com/business/2021/jan/27/eu-covid-vaccines-row-astrazeneca-boss-reveals-problems.

[55] See Bostyn, supra note 1, at 230–58.

[56] AstraZeneca Takes Next Steps Towards Broad and Equitable Access to Oxford University's COVID-19 Vaccine (June 4, 2020), www.astrazeneca.com/content/astraz/media-centre/press-releases/2020/astrazeneca-takes-next-steps-towards-broad-and-equitable-access-to-oxford-universitys-covid-19-vaccine.html.

[57] HALIX Signs Agreement With AstraZeneca For Commercial Manufacture of COVID-19 Vaccine (Dec. 8, 2020), www.halix.nl/2020/12/08/halix-signs-agreement-astrazeneca-commercial-manufacture-covid-19-vaccine/.

[58] Medicines Patent Pool, https://medicinespatentpool.org/.

[59] Adam Houldsworth, No, IP rights Are Not the Barrier to COVID-19 Vaccine Supplies, IAM (Feb. 6, 2021), www.iam-media.com/coronavirus/covid-vaccine-supply-not-about-ip-saturday-opinion.

Another solution to guarantee access to vaccines and therapeutics at reasonable prices is to grant compulsory licenses. In Europe, all Patent Acts provide for compulsory licensing, even though the conditions under which they can be granted may differ across nations.[60] In the United States, Section 1498 enables the federal government to step in and use patents in exchange for reasonable compensation, but this authority has never been invoked in any context, let alone for COVID-19.[61] Compulsory licensing is deeply unpopular in both Europe and the United States, and these statutory schemes are rarely invoked. However, a global pandemic is as good a moment as any to begin using these approaches of last resort.[62]

The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs Agreement) also allows for compulsory licensing,[63] and during health crises, it suspends the usual requirement of exhausting voluntary licensing options prior to the grant of a compulsory license.[64] The details of that framework, however, apply predominantly to domestic supply,[65] except for export to the least-developed countries – those that lack production infrastructure.[66] Even in high-income countries, the technical infrastructure may not exist for manufacturing vaccines, especially vaccines as complex as the COVID-19 mRNA vaccines. The more complex the manufacturing process, the less likely that addressing the intellectual property and regulatory issues alone will enable rapid scale-up of production.[67] More effective mechanisms for transferring the necessary know-how will also have to be considered.[68] A refined statutory framework may be needed to allow for global manufacturing via compulsory licensing. In spite of US support, the United Kingdom and the European Union continue to oppose waivers of IPRs during the pandemic.[69] Given the time required for vaccine scale-up, compulsory licensing needs to occur at earlier stages in development.

Compulsory licenses might resolve patent rights issues and guarantee manufacturing of vaccines and therapeutics, but only if regulatory exclusivities are waived or deferred, an option that does not currently exist.[70] Deferring the practical

[60] See Bostyn, supra note 1, at 262.

[61] Christopher Morten & Charles Duan, Who's Afraid of Section 1498? A Case for Government Patent Use in Pandemics and Other National Crises, 23 *Yale J. L. Tech.* 1 (2020).

[62] See Bostyn, supra note 1, at 261–67.

[63] Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), art. 31, Apr. 15, 1994, 1869 U.N.T.S. 299.

[64] Id. at art. 31(b).

[65] Id. at art. 31(f).

[66] Id. at art. 31(b).

[67] See Derek Lowe, In the Pipeline Blog: Myths of Vaccine Manufacturing, Sci. Translational Med. (Feb. 2, 2021), www.science.org/content/blog-post/myths-vaccine-manufacturing.

[68] See W. Nicholson Price II, Arti K. Rai & Timo Minssen, Knowledge Transfer for Large-Scale Vaccine Manufacturing, 369 *Sci.* 912 (2020).

[69] Adam Lidgett, Groups Warn COVID IP Waiver Could Hurt Pandemic Efforts, Law360 (Mar. 31, 2021), www.law360.com/articles/1370726/groups-warn-covid-ip-waiver-could-hurt-pandemic-efforts.

[70] See Ellen F. M. 't Hoen, Pascale Boulet & Brook K. Baker, Data Exclusivity Exceptions and Compulsory Licensing to Promote Generic Medicines in the European Union: A Proposal for Greater Coherence in European Pharmaceutical Legislation, 10 *J. Pharm. Pol'y Prac.* 19 (2017).

application of regulatory exclusivities, including data exclusivity, would similarly require statutory change. The benefit of a deferral is that those rights could be paused, to be invoked at a later date. Yet deferring exclusivity to a "less acute" period of the COVID-19 pandemic would permit manufacturers to profit now without curtailing the period where they can charge higher prices. This is the situation in the United States: EUAs have slowed momentum toward full approval and licensure of vaccines, and as a result, regulatory exclusivity periods for many vaccines and therapeutics have yet to start.

Vaccine nationalism further complicates the matter by exacerbating disparities in vaccine access – scarce supply goes to the highest bidder, while the rest of the world waits indefinitely.

The United States has committed to more vaccines than it needs, while in low-income countries, access to vaccines has been limited. COVID-19 Vaccines Global Access (COVAX), which is co-led by Gavi,[71] the Coalition for Epidemic Preparedness Innovations, and the WHO, aims to accelerate the development and manufacture of COVID-19 vaccines, and to guarantee fair and equitable access for every country in the world.[72] By early September 2021, COVAX had delivered 240 million doses to 139 countries.[73] Yet even COVAX seems willing to sell vaccines to the highest bidder.[74] Finally, advance purchase agreements could be conditioned on commitments from manufacturers to voluntarily license technology to third-party manufacturers in order to shore up global supply, though this might limit the power of the advance purchase agreement as a pull incentive for innovation.

IV LESSONS FOR THE FUTURE

During the COVID-19 pandemic, the global biopharmaceutical industry has invested considerable time and resources in the development of treatments and vaccines. Since rapid success was so crucial, the industry also received massive support from public resources and investments around the globe, including US and EU public authorities and EU member states. As a result, millions of people have received highly effective vaccines, several promising vaccine candidates are on the horizon, and some therapeutics show promise in mitigating the severity of SARS-CoV-2 infection. In spite of these successes, challenges to global access and affordability remain due to widespread and ongoing inequities. Few of these inequities have been adequately addressed during the COVID-19 pandemic and

[71] Gavi, the Vaccine Alliance, www.gavi.org.

[72] COVAX Facility, www.gavi.org/covax-facility.

[73] See Joint COVAX Statement on Supply Forecast for 2021 and Early 2022 (Sept. 8, 2021), www.unicef.org/press-releases/joint-covax-statement-supply-forecast-2021-and-early-2022.

[74] Paul Karp, Australia's Pfizer Purchase from Vaccine-Sharing Covax Stockpile under Fire, Guardian (Aug. 16, 2021), www.theguardian.com/australia-news/2021/aug/17/australia-pfizer-purchase-from-vaccine-sharing-covax-stockpile-under-fire.

remain substantial obstacles in addressing future pandemics.[75] Inequities have contributed substantially to the prolongation of this pandemic as new SARS-CoV-2 variants continue to emerge for which new booster inoculations will likely be necessary. New variants of contagious viruses are a hallmark of every pandemic, present and future.

This chapter shows that resolving the devastating health issues caused by pandemics tend to follow a similar scenario, convincing those in higher-income nations to subsidize – via pull and push mechanisms – R&D in vaccines and therapeutics. Despite massive public spending, the vaccines and therapeutics are subject to a dense thicket of exclusive rights, in the form of patents, regulatory exclusivities, and trade secrets. The COVID-19 pandemic is no exception.

That web of exclusive rights allows the holders of those rights to act as gatekeepers, restricting access to, and setting the price of, the technology needed to produce vaccines and therapeutics.[76] Despite the existence of competition in the COVID-19 vaccine space, the need to vaccinate billions of people across the globe still gives substantial leverage to the holders of those exclusive rights and presents barriers to access. The recent push to waive IPRs for COVID-19 vaccines illustrates the rather belated realization of the importance of exclusive rights during pandemics.[77] Presumably, a waiver would free those vaccines from their exclusive rights, which could clear a path for third parties to manufacture them – thereby increasing volume while lowering price.[78] Though there are other complex supply chain issues as well, discussions of intellectual property waivers for COVID-19 vaccines understate the complexities of the exclusive rights involved.[79] As noted earlier, COVID-19 vaccines are protected by hundreds of patents, including those that cover the vaccine platforms, and many of the vaccine manufacturing processes are closely guarded

[75] Olivier J. Wouters et al., Challenges in Ensuring Global Access to COVID-19 Vaccines: Production, Affordability, Allocation, and Deployment, 397 *Lancet* 1023 (2021).

[76] Aisling McMahon, Global Equitable Access to Vaccines, Medicines and Diagnostics for COVID-19: The Role of Patents as Private Governance, 47 *J. of Med. Ethics* 142 (2021).

[77] World Trade Org., Council for Trade-Related Aspects of Intellectual Property Rights, Waiver From Certain Provisions of the Trips Agreement for the Prevention, Containment and Treatment of COVID-19, WTO Doc. IP/C/W/669 (2020), revised version WTO Doc. IP/C/W/669/Rev.1 (2021). This has finally been watered down by the Ministerial Decision of June 17, 2022 to an Art. 31bis TRIPS style of compulsory licensing patent waiver, WT/MIN(22)/30 – WT/L/1141.

[78] Siva Thambisetty et al., The TRIPS Intellectual Property Waiver Proposal: Creating the Right Incentives in Patent Law and Politics to End the COVID-19 Pandemic (LSE Legal Studies, Working Paper No. 06/2021, 2021), https://ssrn.com/abstract=3851737.

[79] Sven J.R. Bostyn, Why a COVID IP Waiver Is Not a Good Strategy 5-13 (May 10, 2021), https://ssrn.com/abstract=3843327; Reto M. Hilty et al., COVID-19 and the Role of Intellectual Property Position. Statement of the Max Planck Institute for Innovation and Competition of 7 May 2021, www.ip.mpg.de/fileadmin/ipmpg/content/stellungnahmen/2021_05_25_Position_statement_Covid_IP_waiver.pdf; Duncan Matthews & Timo Minssen, US U-turn on COVID IP Waiver Alone Will Not Solve Vaccine Crisis – Intellectual Property Is an Important Part of the Debate, but Greater Transparency Is Required (May 2021), https://privpapers.ssrn.com/sol3/papers.cfm?abstract_id=3881020.

as trade secrets.[80] Finally, regulatory exclusivities are only partially governed by the TRIPS Agreement and would not entirely fall within the scope of the waiver.

Safeguards are needed to guarantee global access to sufficient vaccines at reasonable prices. Such solutions are even more urgent given the emergence of new SARS-CoV-2 variants. If new booster shots against the variants become necessary, current vaccine-related inequities will surely be replicated if nothing is done. That might require statutory change, such as waiving regulatory exclusivities in compulsory licensing arrangements. Moreover, the use of compulsory licensing should become part of a more sophisticated approach to contractual arrangements, such as in advance purchasing agreements. If negotiated equitably, vaccine developers and manufacturers could be contractually obligated to supply more (as opposed to "best effort" commitments) while granting licenses to third parties that can scale up vaccine production in facilities abroad – with appropriate guarantees of safety and quality. Those contractual arrangements could also require vaccine developers to supply the COVAX system directly, with a view toward eliminating inequities in low- and middle-income countries.

As the development and manufacturing of COVID-19 vaccines (and to some extent COVID-19 therapeutics) has largely been financed by public resources,[81] governments have the leverage to use these tools. This may contrast with other areas of drug development, in which the role of public funding might be more limited. Greater effort should be made toward pooling of vaccine and therapeutics technology, including manufacturing processes; C-TAP has not been optimally utilized during COVID-19.

Although more research is needed, our analysis offers a starting point for broader discussions of the nature of these incentives in Europe and the United States. Our proposed solutions may enable global access to products essential for resolving the COVID-19 pandemic, but can also be broadly applied to future global crises. Careful analyses of the complex dynamics that drive innovation, global manufacturing scale-up, and access are essential for improving pandemic preparedness, pharmaceutical innovation, and global access issues in the future.

[80] See Bostyn, supra note 79, at 6–9; Matthews & Minssen, supra note 79 at 1–2; Ana Santos Rutschman & Julia Barnes-Weise, The COVID-19 Vaccine Patent Waiver: The Wrong Tool for the Right Goal, Bill of Health (May 5, 2021), https://blog.petrieflom.law.harvard.edu/2021/05/05/covid-vaccine-patent-waiver/.

[81] Hussain S. Lalani, Jerry Avorn & Aaron S. Kesselheim, US Taxpayers Heavily Funded the Discovery of COVID-19 Vaccines, 101 *Clin. Pharmacol. Ther.* 542 (2021); see also Bostyn, supra note 79, at 14–16; Duncan Matthews & Timo Minssen, The Prospects for an IP Waiver Under the TRIPS Agreement, Bill of Health (July 6, 2021), https://blog.petrieflom.law.harvard.edu/2021/07/06/the-prospects-for-an-ip-waiver-under-the-trips-agreement/.