World Trade Review (2025), **24**, 302–320
doi:10.1017/S147474562400020X

ORIGINAL ARTICLE

mRNA Technology Transfer Hub and Intellectual Property: Towards a more Equitable and Sustainable Model

Tolulope Anthony Adekola[1] and Bryan Mercurio[2†]

[1]Research Fellow, T.C. Beirne School of Law, University of Queensland, Brisbane, Australia and [2]Simon F.S. Li Professor of Law, The Chinese University of Hong Kong, Hong Kong SAR
Corresponding author: Bryan Mercurio; Email: b.mercurio@cuhk.edu.hk

(Received 29 November 2023; revised 17 March 2024; accepted 18 March 2024; first published online 30 January 2025)

Abstract
The article explores how the COVID-19 pandemic revived discussions on the importance of local pharmaceutical production for promoting health security and resilient health systems. It examines the World Health Organization's hub and spoke mRNA vaccine production model (mRNA hub), a global initiative that aims to establish sustainable, local mRNA manufacturing capabilities in low- and middle-income countries in response to the inequities in access to COVID-19 vaccines and the trade disruptions during the pandemic. Using the mRNA hub as case study, the paper discusses how the tectonic shift towards local production implicates supply and license agreements, and thus IPRs. The paper maps the intellectual property challenges that might impact the mRNA hub's sustainability and provides recommendations on how to enhance the initiative's chances of success and foster a more equitable pharmaceutical sector in the future.

Keywords: TRIPS; vaccines; mRNA; local production; vaccine; equity

1. Introduction

The global health crisis brought about by the COVID-19 pandemic has reignited discussions about the role of local pharmaceutical production[1] in promoting health security and resilient health systems.[2] Throughout the pandemic, the significance of local pharmaceutical production became evident as the demand for vaccines and essential medicines surged worldwide, resulting

[†]RGC Senior Research Fellow (2023–27).

[1]Local production refers to the creation of capacity with an emphasis on the geographical location rather than production efficiency. See P.G. Sampath and J. Pearman (2021) 'Local Production of COVID-19 Vaccines: A Strategy for Action', *Global Policy*, August, 2021, www.globalpolicyjournal.com/sites/default/files/pdf/Gehl%20Sampath%20and%20Pearman%20-%20Local%20Production%20of%20COVID%2019%20Vaccines%2C%20A%20Strategy%20for%20Action_0.pdf); A. Seiter (2005) 'Pharmaceuticals: Local Manufacturing (HNP Brief #3)', March 2005, https://documents1.worldbank.org/curated/en/358631468008448574/text/321930HNPBrief130Pharmeceuticals.txt).

[2]See F.M. Abbott and J.H. Reichman (2020) 'Facilitating Access to Cross-Border Supplies of Patented Pharmaceuticals: The Case of the COVID-19 Pandemic', *Journal of International Economic Law* 23(3), 535–561; See also W. Fisher, R.L. Okediji, and P.G. Sampath (2022) 'Fostering Production of Pharmaceutical Products in Developing Countries', *Michigan Journal of International Law* 43, 1; O.J.Wouters, K.C. Shadlen, M. Salcher-Konrad, A.J. Pollard, H.J. Larson, Y. Teerawattananon, and M. Jit (2021) 'Challenges in Ensuring Global Access to COVID-19 Vaccines: Production, Affordability, Allocation, and Deployment', *The Lancet* 397(10278), 1023–1034.

in supply chain disruptions and shortages of critical products.[3] While a few countries with established production capabilities were better equipped to meet the needs of their populations, others faced vulnerability due, in part, to export restrictions on scarce medical technologies.[4] The shocking impact of the pandemic, therefore, led many countries to begin to consider local pharmaceutical production as a means of reducing dependence on external sources for supply.[5] This consideration became even more prominent due to the severe consequences of the pandemic on the political stability and socio-economic fabric in many countries, raising genuine concerns about national security and the compelling imperative of building a self-sustaining local pharmaceutical sector.[6]

In most instances, the notion of local production is associated with building capacity in underserved, developing country markets. But the pandemic, coupled with increasing trade tensions and Russia's invasion of Ukraine, has broadened the scope, and high-income countries are also interested in building local production capacity. For instance, disruptions in the pharmaceutical supply chain during the pandemic triggered concerns about the sustainability of outsourcing active pharmaceutical ingredient (API) production to Asia in both the United States and the European Union.[7] This general concern is exasperated by specific concerns relating to reliance on China for a large percentage of APIs.[8] For instance, since 2020, US imports of Chinese pharmaceuticals (defined by the US tariff code to include packaged medicaments, vaccines, blood, organic cultures, bandages, and organs) has grown by 485%, going from $2.1B in 2020 to $10.3B in 2022.[9] These concerns led to the EU, in April 2023, adopting a proposal for a new Directive and a new Regulation which revise and replace the existing general pharmaceutical legislation.[10] Ongoing discussions focus on policy measures such as reshoring pharmaceutical production, specifically active pharmaceutical ingredient manufacturing, back to Europe to strengthen the pharmaceutical supply chain and protect 'pharmaceutical sovereignty'.[11]

While local production in low- and middle-income countries has been much discussed over the past two decades, the development of local pharmaceutical manufacturing capacity was not considered a priority for advancing these countries' public health agenda in the pre-COVID-19 world for two reasons. First, accessing medicines at prices close to the marginal costs of production was seen as the best way to serve the population regardless of whether the medicines were imported or locally produced.[12] Substantial price reductions introduced by Indian companies during the HIV/AIDS crisis and subsequently by Chinese companies through the expansion of generic drug production meant that it made little economic sense to either try to

[3]See P.G. Sampath (2022) 'Trade Measures on Pharmaceutical Products: Can They Promote Local Production and Public Health?', *Asia-Pacific Sustainable Development Journal* 29(2), 234–234.

[4]Ibid.

[5]T. Meyer (2020) 'Trade Law and Supply Chain Regulation in a Post-COVID-19 World', *American Journal of International Law* 114(4), 637–646.

[6]See S.M. Malik, A. Barlow, and B. Johnson (2021) 'Reconceptualising Health Security in Post-COVID-19 World', *BMJ Global Health* 6(7), e006520; See also A. Elnaiem, O. Mohamed-Ahmed, A. Zumla, J. Mecaskey, N. Charron, M.F. Abakar, and O. Dar (2023) 'Global and Regional Governance of One Health and Implications for Global Health Security', *The Lancet*.

[7]See European Commission, 'A Pharmaceutical Strategy for Europe', https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe_en.last (last accesssed 26 July 2023).

[8]See B. Mercurio and R. Tundage (2023) 'Balancing Global Interdependence and Self-Reliance: The Future of Critical Medicines Production', Think Global Health, www.thinkglobalhealth.org/article/balancing-global-interdependence-and-self-reliance?utm_source=tw_tgh&utm_medium=social_owned (last accessed 26 July 2023).

[9]N. Graham 'The US is Relying more on China for Pharmaceuticals – and Vice Versa, Atlantic Council', Atlantic Council, www.atlanticcouncil.org/blogs/econographics/the-us-is-relying-more-on-china-for-pharmaceuticals-and-vice-versa/ (last accessed 26 July 2023).

[10]Supra n. 7.

[11]Ibid.

[12]W. Kaplan and R. Laing (2005) 'Local Production of Pharmaceuticals: Industrial Policy and Access to Medicines – an Overview of Key Concepts, Issues, and Opportunities for Future Research', The World Bank.

https://doi.org/10.1017/S147474562400020X Published online by Cambridge University Press

compete or to build domestic capacity at a higher cost. Second, concerns were raised about large-scale market failures in low-income countries resulting from underdeveloped markets, inadequate infrastructure, lack of a skilled workforce, regulatory barriers, and low institutional support.[13]

However, the pandemic has resulted in a tectonic shift in thinking with the narrative now that local production must become a reality.[14] With the emergence of health nationalism, rising trade barriers, and the absence of regional manufacturing capabilities to guarantee supply in a crisis, safeguarding low- and middle-income countries' health in a sustainable way is now thought to be achievable by fostering its ability to manufacture the health products it needs to address public health emergencies.[15]

It is against this background that the mRNA technology transfer hub (mRNA hub) was initiated by the World Health Organization (WHO) in response to the inequities in access to COVID-19 vaccines and the trade disruptions during the pandemic.[16] Its goal is to establish sustainable, local mRNA manufacturing capabilities by working with a network of technology recipients (known as spokes) in low- and middle-income countries.[17] While the goals of the mRNA technology transfer hub are commendable, building production capacity in low-resource contexts presents challenges. In most low- and middle-income countries, for example, establishing a robust vaccine manufacturing industry requires capital investment (public and private), technology transfer, and business strategies that align with vaccine demand.[18] Additionally, quality assurance, stringent and independent regulatory review, resilient supply chains, and supportive industries and systems need to be in place prior to production.[19] Even if these conditions and challenges are surmounted, historical experiences of firms engaged in production in most low- and middle-income countries show that recouping investments and breaking even depend not only on technological and industrial upgrading and finance but also on guaranteed access to markets without being undercut by global competitors.[20]

Apart from the previously mentioned constraints, navigating the intellectual property rights (IPRs) landscape poses a significant hurdle for local vaccine production and, in this case, the mRNA hub and its spokes. Yet the heavily debated TRIPS waiver proposal for COVID-19 vaccines and treatments, which resulted in the Ministerial Decision on the TRIPS Agreement[21] at the World Trade Organization (WTO), provided little or no benefit for initiatives like the mRNA hub to facilitate sustainable local production capacity building and significantly mitigate the potential intellectual property threats to access.[22] However, the pandemic has proven to be a

[13]See R. Bate (2008) 'Local Pharmaceutical Production in Developing Countries', *Campaign for Fighting Diseases*, www.libinst.ch/publikationen/LI-LocalPharmaceuticalProduction.pdf.

[14]P. Steele, G.K.M. Ali, A. Levitskiy, and L. Subramanian (2020) 'A Case for Local Pharmaceutical Manufacturing in Africa in Light of the COVID-19 Pandemic', Pamale Steele and Associates.

[15]See A. Irwin (2021) 'How COVID Spurred Africa to Plot a Vaccines Revolution', *Nature (Lond.)*; See also A.M. Ekströ, G. Tomson, R.K. Wanyenze, Z.A. Bhutta, C. Kyobutungi, A. Binagwaho, and O.P. Ottersen (2021) 'Addressing Production Gaps for Vaccines in African Countries', *Bulletin of the World Health Organization* 99(12), 910. See also A.A. Saied, A.A. Metwally, M. Dhawan, O.P. Choudhary, and H. Aiash (2022) 'Strengthening Vaccines and Medicines Manufacturing Capabilities in Africa: Challenges and Perspectives', *EMBO Molecular Medicine* 14(8), e16287.

[16]See World Health Organization, *The mRNA Vaccine Technology Transfer Hub*, www.who.int/initiatives/the-mrna-vaccine-technology-transfer-hub (last accessed 26 July 2023).

[17]Ibid.

[18]See Saied, supra n. 15.

[19]Ibid.

[20]S. Chaudhuri, M. Mackintosh, and P.G. Mujinja (2010) 'Indian Generics Producers, Access to Essential Medicines and Local Production in Africa: An Argument with Reference to Tanzania', *The European Journal of Development Research* 22, 451–468.

[21]WTO, 'Draft Ministerial Decision on the TRIPS Agreement', Ministerial Conference', 12th Session, WT/MIN(22)/W/15/Rev.2 (17 June 2022).

[22]For discussions on the TRIPS waiver for COVID-19 Vaccines and Treatments at the WTO which revolves around expanding the scope of compulsory licenses in article 31bis, See B. Mercurio and P.N. Upreti (2022) 'From Necessity to Flexibility: A Reflection on the Negotiations for a TRIPS Waiver for COVID-19 Vaccines and Treatments', *World Trade*

https://doi.org/10.1017/S147474562400020X Published online by Cambridge University Press

major trade disruption which has shifted the narrative and will lead to a reorientation of trade flows and the entire pharmaceutical production landscape away from pure cost-based efficiency and towards a more equitable and sustainable model.

This article aims to map the intellectual property issues that may impact the mRNA hub's sustainability and explore potential strategies for addressing them. This is crucial for three important reasons. First, many third-party players involved in mRNA research and development assert their IPRs over the mRNA 'commons,' and these players are not bound by the same terms as the hub agreements.[23] This raises questions about the feasibility and desirability of pure 'open access' within the mRNA space. Second, the Medicines Patent Pool (MPP) and WHO do not guarantee freedom to operate at the country level where the 'spokes'[24] are located but only provide an intellectual property landscape analysis specific to each country.[25] Simply stated, it is the responsibility of the hub, each 'spoke', and the export markets to confirm the actual status and scope of patents/claims filed and/or granted in their respective country.[26] Third, while voluntary licensing is the intended method for accessing patented mRNA technologies for the hub and spokes, the complex mRNA patent landscape may necessitate consideration of other instruments of access within patent law. Hence, the article proceeds as follows: section 2 provides an overview of the mRNA technology hub and its current model as well as the implications of the growing mRNA patent landscape on the freedom to operate within the mRNA hub initiative; section 3 maps out relevant intellectual property related factors and strategies that, under different conditions, might impact the mRNA Hub's sustainability. Section 4 concludes with general recommendations.

2. Overview and Design Features of the mRNA Technology Transfer Hub

On 21 June 2021, the WHO, the MPP, and the Act-Accelerator/COVAX launched the mRNA technology transfer hub to enhance the manufacturing capacity of low- and middle-income countries in producing mRNA vaccines.[27] The hub, known as the mRNA Vaccine Technology Hub or mRNA hub, is located in South Africa and consists of Afrigen Biologics, the South African Medical Research Council (SAMRC), and Biovac.[28] Within this consortium, Afrigen is responsible for establishing mRNA vaccine production technology, SAMRC contributes to research, and Biovac serves as the initial manufacturing 'spoke'.[29] The program thus operates on a hub-and-spoke model with the main function being to advance mRNA technology, scale up vaccine production, and conduct testing in accordance with Good Manufacturing Practices.[30] Additionally, the hub serves as a training centre for spokes, providing technology transfer materials and assistance throughout the transfer process.[31] However, are responsible

Review 21(5), 633–649; see also R. Hilty, D. Kim, J.I. Correa, P.H.D. Batista, and M. Lamping (2022) 'Position Statement of 5 July 2022 on the Decision of the WTO Ministerial Conference on the TRIPS Agreement adopted on 17 June 2022', Max Planck Institute for Innovation & Competition Research Paper (22-14).

[23]See M. Davies (2022) 'Covid-19: WHO Efforts to Bring Vaccine Manufacturing to Africa Are Undermined by the Drug Industry, Documents Show', BMJ, 376; see also S. Ali, A. Jacub, and S. Stranges (2023) 'COVID-19 Vaccine Inequity and Big Pharma: Time to Rethink Our Love Affair?', *Canadian Journal of Public Health* 114(1), 80–81.

[24]In the context of the mRNA hub initiative, a 'spoke' is a manufacturing facility in a low- or middle-income country that receives technology transfer from the hub to produce mRNA vaccines.

[25]See Section 3.4 and 10.2 of the 'mRNA Technology Transfer Spoke Agreement Template', https://medicinespatentpool.org/what-we-do/mrna-technology-transfer-programme/agreements#pills-Partners--Agreements

[26]Ibid.; see also WHO lecture on Technology sharing and managing collective knowledge within the WHO mRNA technology transfer Hub delivered on 16 January 2023, https://dndi.org/wp-content/uploads/2023/01/ParkC-Workshop-HealthCommonsApproachPandemicPrepardness-16Jan2023.pdf.

[27]World Health Organization, supra n. 16.

[28]Ibid.

[29]Ibid.

[30]See Medicines Patent Pool, mRNA Technology Transfer Programme, https://medicinespatentpool.org/what-we-do/mrna-technology-transfer-programme.

[31]Ibid.

https://doi.org/10.1017/S147474562400020X Published online by Cambridge University Press

Table 1. Recipients of mRNA technology from the WHO mRNA technology transfer hub (WHO)

Country	mRNA technology recipient
Argentina	Sinergium Biotech
Brazil	Bio-Manguinhos
Egypt	BioGeneric Pharma S.A.E
Kenya	tbd*
Nigeria	Biovaccines Nigeria Limited
Senegal	Institut Pasteur de Dakar
Tunisia	Institut Pasteur de Tunis
Bangladesh	Incepta Vaccine Ltd
Indonesia	Biofarma
India	BiologicalE (Bio E)
Pakistan	National Institute of Health
Serbia	Institut Torlak
South Africa	Biovac
Ukraine	Darnitsa
Viet Nam	Polyvac

for developing a viable business model. This includes securing upfront financing, establishing the necessary infrastructure and workforce for mRNA technology, receiving technology transfers from the hub according to an agreement with the MPP, and implementing and expanding the technologies according to their specific requirements.[32]

The WHO leads global coordination and monitoring of the initiative, while the MPP provides support on intellectual property matters.[33] Over 40 countries have expressed interest in acquiring the developed technology.[34] Currently, the WHO has announced that 15 manufacturers (spokes) in Egypt, Kenya, Nigeria, Senegal, South Africa, Tunisia, Indonesia, Brazil, Argentina, Pakistan, India, Vietnam, Bangladesh, Serbia, and Ukraine will receive technology transfers through the mRNA hub Table 1.

Training for the first set of spokes began in March 2022, and commercialization of vaccines produced by the South African hub is expected to start by the end of 2024.[35] Additionally, the WHO acknowledges that technology transfer alone is insufficient within the broader context of promoting local production given two major barriers – limited availability of a trained workforce and weak regulatory capacity. The WHO is attempting to address these barriers by establishing biomanufacturing workforce training centres and collaborating with the WHO Academy to ensure that regulatory and biomanufacturing training meet the needs and objectives of the countries.[36]

Moreover, the demonstrated efficacy of mRNA vaccines against COVID-19 makes them a significant focus for the mRNA technology transfer hub. The unprecedented success story of mRNA technology, during the pandemic, positions it as an attractive area for further development and exploration. Despite being a relatively new technology, mRNA is said to offer ease of sharing,

[32]Ibid.
[33]World Health Organisation, supra n. 16.
[34]Ibid.
[35]Ibid.
[36]Ibid.

https://doi.org/10.1017/S147474562400020X Published online by Cambridge University Press

development, and adaptation to address other diseases including HIV/AIDs, cancer, rare diseases, malaria, and tuberculosis.[37] As such, the hub is projected to yield long-term benefits for regions where the spokes are established, particularly those underserved by the global pharmaceutical market.[38] In general, the hub appears to offer a revitalizing and ambitious alternative to the current approach to vaccine development and distribution, which was starkly exposed as having vulnerabilities during the pandemic.

2.1 The Intellectual Property Challenges

IPRs are at the core of the mRNA hub's activities. The MPP is to assist, with its expertise in intellectual property management, by providing analysis and defining and negotiating terms and conditions of eventual agreements.[39] The intellectual property arrangement is that Afrigen will grant MPP a non-exclusive license to utilize its data and inventions to achieve the goals of the initiative.[40] Under this understanding, the MPP is authorized to share the program data with the WHO and third parties.[41] The MPP will then enter into an agreement with the spokes whereby it grants each spoke a non-exclusive license to develop and commercialize 'products' based on the technology developed by the hub.[42] Each spoke will in turn grant to MPP and other spokes a non-exclusive license to any data or inventions it develops based on the technology transferred by the hub.[43]

The key issue regarding the intellectual property arrangement is that MPP and WHO do not guarantee freedom to operate in the spoke's territory and export markets. Instead, they only provide an intellectual property landscape analysis at the spoke's country level. Consequently, the responsibility of confirming the actual status and scope of patents/claims filed and/or granted in the spoke's country lies with the spokes. Section 10.2 of the mRNA Vaccines Technology Transfer template agreement between MPP and the spokes is very clear on this point:

> Furthermore, nothing in this Agreement shall be construed as a warranty that [XXX]'s use of the Technology, Afrigen Rights, or Biovac Rights will not infringe any patent rights or other IP rights of any Third Party. MPP does not give any warranty, express or implied, with regard to the safety or efficacy of any Product(s), and it shall be the sole responsibility of [XXX] to ensure such safety or efficacy.

The above provision, while understandable due to the territoriality of intellectual property law, suggests that the spokes need to be aware of and take into account any existing patents or IPRs in their territory that could impact the activities of the initiative as a whole. The complexity of this understanding has already become apparent. For instance, the mRNA hub (Afrigen) located in Cape Town has already been accused of infringing on Moderna's patent for the mRNA COVID-19 vaccine which is currently in force in South Africa.[44] In response to the accusation, the MPP stated that its model of public health licensing relies on the voluntary participation of intellectual property holders, and, thus, it has no intention of engaging in any patent

[37]See Bryce, E. and S. Ong (2022) 'Covid-19 and mRNA Technology are Helping Africa Fix Its Vaccine Problems', BMJ, 377.

[38]See A.A. Saied (2022) 'mRNA Vaccines and Clinical Research in Africa: From Hope to Reality', *International Journal of Surgery (London, England)* 105: 106833.

[39]Medicines Patent Pool, supra n. 29.

[40]See Agreement between Medicines Patent Pool and Afrigen Biologics (Pty) Ltd, https://medicinespatentpool.org/what-we-do/mrna-technology-transfer-programme/agreements#pills-Agreements-of-Consortium.

[41]Ibid.

[42]See The mRNA Technology Transfer Spoke Agreement Template, supra n. 24.

[43]Ibid., Section 6.2.

[44]See the Medicines Patent Pool Position statement, https://medicinespatentpool.org/news-publications-post/mpp-position-statement-on-patents-with-regards-to-the-mrna-vaccine-technology-transfer-hub.

https://doi.org/10.1017/S147474562400020X Published online by Cambridge University Press

infringement.[45] While it is true that Moderna did not grant a license to the MPP for the hub's activities, MPP has stated that it relied on two grounds to justify its continued use of Moderna's mRNA technology without consent.[46] First, is that the patent law in South Africa contains a research exception provision authorizing R&D activities in the country, regardless of any patent situation.[47] Second, is that Moderna has committed not to enforce its COVID-19-related patents against low- and middle-income countries developing vaccines to combat the pandemic.[48]

Both of these justifications are thin, if not without merit. First, far from having an all-encompassing experimental use/research exception, South Africa's Patent Act only contains a narrow regulatory review exception – that is, the exception is limited to the purposes of applying for regulatory/marketing approval – that is specifically limited to non-commercial use. Section 69A of the South African patent law reads:

> (1) It shall not be an act of infringement of a patent to make, use, exercise, offer to dispose of, dispose of or import the patented invention on a non-commercial scale and solely for the purposes reasonably related to the obtaining, development and submission of information required under any law that regulates the manufacture, production, distribution, use or sale of any product.
>
> It shall not be permitted to possess the patented invention made, used, imported or acquired in terms of subsection (1) for any purpose other than for the obtaining, development or submission of information as contemplated in that subsection.

This is a contradistinction to an actual experimental use/research exception, an example of which is Article 47(3) of the Indian Patent Act which subjects the grant of a patent to the condition that:

> any machine, apparatus or other article in respect of which the patent is granted or any article made by the use of the process in respect of which the patent is granted, may be made or used, and any process in respect of which the patent is granted may be used, by any person, for the purpose merely of experiment or research including the imparting of instructions to pupils.

It is generally assumed that Article 47(3) falls within the scope of Article 30 of the TRIPS Agreement, a broadly worded provision allowing WTO Members to provide exceptions to the patent owner's exclusive rights, provided that such exceptions are limited, do not unreasonably conflict with a normal exploitation of the patent, and do not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties.[49]

Moreover, while it is true to Moderna had committed to not enforcing its COVID-19 related patents against those making vaccines intended to combat the pandemic, the commitment was temporal in nature and limited to 'while the pandemic continues'. With COVID-19 ceasing to be a pandemic, the commitment would have been no longer in place. To its credit, however, Moderna recently voluntarily pledged 'to never enforce patents related to its COVID-19 vaccines against companies manufacturing in or for the 92 low- and middle-income countries in the Gavi COVAX Advance Market Commitment (AMC), provided that the manufactured vaccines are

[45]Ibid.

[46]Ibid.

[47]Ibid. Note that Section 69(A)(1) of the Patents Act, which was introduced in 2002, prescribes certain non-infringing acts. For example, it is not an act of infringement to make, use, exercise, offer to dispose of, dispose of, or import a patented invention on a non-commercial scale solely for purposes reasonably relating to obtaining, developing, or submitting the information required under any law regulating the manufacture, production, distribution, use or sale of any product.

[48]Ibid.

[49]See Article 30 of the TRIPS agreement.

https://doi.org/10.1017/S147474562400020X Published online by Cambridge University Press

solely for use in the AMC 92 countries'.[50] Moderna subsequently confirmed that the mRNA hub comes within the scope of the pledge.[51]

Nevertheless, the aforementioned situation generates uncertainty and emphasizes a noteworthy challenge concerning intellectual property for both the hub and the spokes as the initiative advances and begins researching into other diseases and viruses beyond SARS-CoV-2 (COVID-19). This challenge becomes even more intricate due to the complex nature of mRNA technologies, which encompass various patentable aspects such as mRNA sequences, modified nucleotides or bases, delivery systems, manufacturing processes, and therapeutic applications.

It is worth emphasizing that a large part of the uncertainty is not the result of the international legal framework but from inaction at the domestic level and the failure to make use of existing flexibilities in TRIPS. That such research can be conducted in a more secure manner is proof, contrary to the often widely held notion that TRIPS flexibilities are not workable, that they are indeed potent and can be used when needed.

While the underlying reasoning behind the research exception is to facilitate experimentation and research on existing patented technologies thereby advancing the objectives of the patent system, the scope of the exemption varies widely between and among WTO Members whose domestic legislation contains such an exception. In certain jurisdictions, the exception is defined narrowly, while in others it is relatively broad.[52] There have been limited efforts thus far to establish a standardized and widely shared best practices approach across countries, possibly due to the existing differences and challenges associated with such harmonization.

To avoid guard against litigation and unnecessarily narrow interpretation of the exception, the mRNA hub and the countries/regions where the spokes are located should carefully draft an experimental use provision that clarifies the extent to which research and other public health-related activities are exempted from patent infringement liability. A broad provision, perhaps following the Indian example, will ensure that the delineations of the experimental use exemption are clear and wide enough to cover issues such as permitted acts, products, submissions in other jurisdictions, temporal limitations, and limitations to generics or a broader exception employing models that match broad research, public domain, and competition policies in their country.[53] In the absence of a clear experimental use exemption, the activities of the mRNA hub may likely incur unnecessary costs and societal costs, which include possible adverse effects on competition within the mRNA technology space and public health.

2.2 Freedom to Operate

As highlighted in the previous section, the sustainability of the mRNA hub-spoke model is not without intellectual property obstacles. Its freedom to operate would undoubtedly be (in fact is) threatened by, among other reasons, the apparent reluctance of key biotech companies in the

[50]'Moderna's Updated Patent Pledge', https://investors.modernatx.com/Statements--Perspectives/Statements--Perspectives-Details/2022/Modernas-Updated-Patent-Pledge/default.aspx (accessed 18 August 2023)..

[51]POLITICO, 'Moderna to Share Vaccine Tech, Commits to Never Enforce COVID-19 Jab Patents', 8 March 2022, www.politico.eu/article/moderna-share-vaccine-tech-never-enforce-covid19-patents/.

[52]See B. Mercurio (2018) *Drugs Patents and Policy: A Contextual Study of Hong Kong*. Cambridge University Press, 116. In contrast to the wide exception contained in Article 47(3) of India's Patent Act is the United States, which applies a highly restricted and precise exception not through statute but rather common law. In the US, the exception is upheld only in cases where actions are performed for amusement, idle curiosity, or strictly philosophical inquiry, but not when the infringing activities are considered part of the alleged infringer's legitimate business. For example, in the case of *Madey v. Duke* University, the court determined that the experimental use of a patent aligns with the university's 'legitimate business' objectives, which involve educating and enlightening students, faculty participation in research projects, and enhancing the university's reputation to attract grants, students, and faculty. Such a narrow interpretation of the common law privilege significantly diminishes the value of the exception, resulting in it being 'rarely sustained'. Ibid.

[53]For further discussions, see S. O'Connor (2009) 'Enabling Research or Unfair Competition? De Jure and De Facto Research Use Exceptions in Major Technology Countries', in T. Takenka (ed.), *Patent Law and Theory: A Handbook of Contemporary Research*. Edward Elgar.

https://doi.org/10.1017/S147474562400020X Published online by Cambridge University Press

mRNA space to support the initiative. This threat is further aggravated by the growing landscape of mRNA patents. Currently, several companies hold patent portfolios on various components of mRNA technology.[54] Some notable examples include Moderna, BioNTech, CureVac, Arcturus Therapeutics, Alnylam Pharmaceuticals, Translate Bio, Sanofi, GlaxoSmithKline, Pfizer, and Johnson & Johnson.[55] These companies have filed for and been granted multiple claim types that define the boundaries of protected mRNA inventions, covering aspects such as the mRNA sequence itself, the delivery system for mRNA vaccines, the dosage regimen, the medical uses, and the manufacturing processes in many jurisdictions.[56] Recent research analyzing mRNA vaccine patent landscape reveals increasing number of applications in a host of countries, including the United States, China, Japan, the European Patent Office (EPO), South Korea, Australia, India, and South Africa.[57]

Moderna, whose technology the mRNA hub reverse-engineered and produced, did not voluntarily license its technology to the hub. Despite Moderna having filed and been granted several mRNA patents in South Africa, it refused to cooperate and share technology with the hub, likening the replica vaccine produced to a 'copy of a Louis Vuitton handbag'.[58] Instead, Moderna is investing $US500 million in developing a production facility of its own in Kenya.[59] While the activity of Moderna in Kenya is laudable to the extent that it would expand the existing supply source for mRNA-based products, its implication on the mRNA hub's business model is still unclear.

That said, the mRNA patent landscape has been described as a complex and dense 'jungle,' resulting in what is known as a 'patent thicket' – a collection of partially overlapping patent rights that require those seeking to commercialize the technology to obtain permission from multiple rights holders.[60] This situation is similar to the concept of the 'anticommons,' where ownership rights are fragmented among multiple parties, making it difficult to coordinate usage rights necessary to utilize a technology. While the assumption that more patents promote innovation is debatable, a high concentration of patents in the mRNA technology field is likely to discourage the hub's efforts to facilitate technology diffusion and follow-on innovation.[61]

Patent thickets and anticommons have long been on the policy radar. Previous studies have identified factors that can lead to 'bargaining failure', including high transaction costs due to fragmented patent ownership and stacking licenses, as well as information asymmetries and uncertainties about the scope of patent protection.[62] High transaction costs arise not only due to the multiplicity of rights holders but also because of complex freedom-to-operate searches and rights clearance procedures. Licensing mRNA technology patents, given the complexity of the patent landscape, clearly falls into this category and could affect the goal of making affordable

[54]M. Li, J. Ren, X. Si, Z. Sun, P. Wang, X. Zhang, K. Liu, and B. Wei (2022) 'The Global mRNA Vaccine Patent Landscape', *Human Vaccines & Immunotherapeutics* 18(6), 2095837; See also M. Gaviria and B. Kilic (2021) 'A Network Analysis of COVID-19 mRNA Vaccine Patents', *Nature Biotechnology*, 39(5), 546–548.

[55]See H.L. Zhang (2023) 'Current Status and Patent Prospective of Lipid Nanoparticle for mRNA Delivery', *Expert Opinion on Therapeutic Patents* 33(2), 125–131.

[56]G. Aquino-Jarquin (2022) 'The Patent Dispute Over the Breakthrough mRNA Technology', *Frontiers in Bioengineering and Biotechnology* 10.

[57]Ibid.

[58]The Guardian News, '"Like copying a Louis Vuitton handbag": Big Pharma Hits Out at Africa's Replica Covid Vaccine', www.theguardian.com/global-development/2022/oct/05/covid-vaccine-inequity-south-africa-afrigen-mrna (accessed 21 July 2023).

[59]See Reuters, Moderna to build mRNA vaccine manufacturing facility in Kenya, www.reuters.com/business/healthcare-pharmaceuticals/moderna-build-mrna-vaccine-manufacturing-facility-kenya-2022-03-07/ (last accesed 20 July 2023).

[60]J. Ren, X. Zhang, X. Si, X. Kong, J. Cong, P. Wang, X. Li, Q. Zhang, P. Yao, M. Li, Y. Cai, Z. Sun, K. Liu, and B. Wei (2023) 'The Race of mRNA Therapy: Evidence from Patent Landscape', arXiv preprint arXiv:2303.00288.

[61]D. Kim, R. Hilty, E. Hofmeister, P.R. Slowinski, and M. Steinhart (2022) 'CRISPR/Cas Technology and Innovation: Mapping Patent Law Issues', Max Planck Institute for Innovation & Competition Research Paper (22-06).

[62]Ibid.

https://doi.org/10.1017/S147474562400020X Published online by Cambridge University Press

mRNA-based vaccines and therapeutics available in low- and middle-income countries. Even when licensing agreements are reached, the terms could include 'reach-through' provisions. The term 'reach-through' licensing agreements, also known as 'stacking licenses,' describes situations where the owner of an 'upstream' technology patent requires a share of the economic benefits generated through the downstream use of the licensed technology.[63] This exercise of bargaining power makes licensing unappealing to potential licensees (the spokes in this instance), as it allows the patent owner to claim a share in the economic benefits generated downstream under contractual terms. These conditions are likely to result in higher prices for the final products, affecting the hub's goals and sustainability.

Furthermore, in discussions on mRNA patents, one often encounters critical arguments regarding the 'too broad' scope of patent protection afforded to mRNA technologies.[64] Researchers contend that 'extremely broad claims surrounding mRNA technologies have the potential to stifle innovation in the field' and that uncertainty about the 'intellectual property landscape surrounding the technology more generally presents a barrier to entry for researchers and technology developers wishing to explore the technology in their experimental systems of choice.'[65] The argument concerning an 'unduly' broad patent scope raises a different concern: whether what is claimed within a patent is commensurate with the actual contribution to the technological state of the art. As Lord Justice Jacob once observed,

> any product claim is apt to give the patentee '*more than he has invented*' … in two ways. Firstly such a claim will have the effect of covering all ways of making the product including ways which may be inventive and quite different from the patentee's route. Secondly, it will give him a monopoly over all uses of the patented compound, including uses he has never thought of.[66]

The question of whether mRNA patents might claim 'more than invented' should be examined in terms of the sufficiency-of-disclosure requirement. Overall, granting broad claims in the field of mRNA technology could potentially give patent owners excessive control, which may hinder further innovation and competition. Therefore, patent offices must uphold the integrity and effectiveness of the patent system by conducting thorough examinations. A meticulous examination of patent examination no doubt, plays a critical role in ensuring that patents are only granted for genuine inventions that meet the legal requirements for patentability and public policy objectives.[67]

Here again, South Africa's regulations are lacking as it is a non-examining country – that is to say, there is no patent examination in South Africa. Instead, a complete (and formally valid) patent application will lead to the granting of a patent without any check on whether the substantive requirements of patentability are met. The patent will be presumed valid until proven otherwise and may be subject to revocation based on an objection by a third party. Such a process is inimical to controlling excesses, ensuring only 'good' patents are granted and encouraging experimentation and technological development. However, it is important to acknowledge that patent offices in most less-developed countries encounter various challenges, such as limited human resources for examination, a surge in patent applications across diverse technical fields, backlogs,

[63]See K.A. Stafford (2005) 'Reach-Through Royalties in Biomedical Research Tool Patent Licensing: Implications of NIH Guidelines on Small Biotechnology Firms', *Lewis & Clark Law Review* 9, 699.

[64]C. Martin and D. Lowery (2020) 'mRNA Vaccines: Intellectual Property Landscape', *Nature Reviews Drug Discovery* 19 (9), 578–579.

[65]Ibid.

[66]*Lundbeck v Generics Ltd.* [2008] EWCA Civ 311, para 54 (emphasis added).

[67]N. Syam (2022) 'Robust Patent Examination or Deep Harmonization? Cooperation and Work Sharing between Patent Offices', *Access to Medicines and Vaccines: Implementing Flexibilities Under Intellectual Property Law*. Springer International Publishing, 241–276.

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and the pressure to process applications promptly.[68] To address these issues, the countries/regions where the spokes are located could explore entering agreements to outsource examination tasks to more resourceful patent offices or put in place regional patent examination mechanisms that would ensure that their flexibility under the TRIPS Agreement are safeguarded and effectively maintained.

3. Strategies for Navigating the Intellectual Property Complexities

3.1 Patent Law and Policy in the Balance

Against the background of the issues identified in previous sections, the question remains whether intellectual property is a problem or a solution. There are no simple answers to this question: finding the solutions will be a matter of continuing dialogue and cooperation, both within the international community on the policy plane and at a practical level on the part of each spoke. The task of assessing the complex factual situation, and of sifting through a welter of policy options, is immense, necessitating widespread collaboration and the pooling of diverse expertise. In addition, leveraging and utilizing all the flexibilities provided within the international intellectual property framework would also help ensure that the hub delivers on its mandate.[69]

Before commencing manufacturing operations for a particular vaccine, the spokes would need to determine whether any specific patents might present a business risk (that is, patent infringement liability) in the country where their products would be manufactured or sold. Evaluating patent risk is a standard business assessment routinely undertaken by pharmaceutical enterprises, including generic product manufacturers in middle-income countries (such as India). That said, whether patent law is viewed as a problem or a solution would primarily depend on the perspective taken, either an informed and strategic view or a reactive one. The essential logic of the patent system is often portrayed as a 'balance': an optimal balance that respects the private interests of those investing resources in the development of new technologies and that promotes the broader public interest in seeing these new technologies emerge not only as abstract scientific publications but as effective, proven technologies that are actually disseminated to the broader public, for overall welfare outcomes.[70] Achieving this idea of 'balance' is complex in the context of the mRNA technology transfer hub; but, broadly speaking, the complexity can be neatly navigated by addressing some key pre-patent grant and post-patent grant issues for mRNA technologies.

In the pre-grant phase for mRNA technologies, the primary concern of the countries and regions where the spokes are located should be to ensure that the patents granted are in the public interest, as defined by the 'patentability' criteria.[71] These would ensure that mRNA patents are only granted for technologies that are genuine additions to existing technological knowledge (i.e., 'novel'), involve a significant advancement in their technical field (i.e., 'inventive' or 'non-obvious'), and are practically useful (i.e., have 'utility' or 'industrial applicability').[72] For mRNA technologies, the patent offices must particularly ensure that the patent applications describe the invention in enough detail for someone skilled in the field to replicate it, which is what makes patent information systems valuable. The scope of the patent rights claimed should not exceed the new technology disclosed in the patent, and patent offices should narrow claims during the application phase to ensure that patent rights are limited to their proper scope.[73]

[68]Ibid., 243.

[69]For discussions on TRIPS flexibilities, see B. Mercurio, T.A. Adekola, and C.F. Tsega (2023) 'Pharmaceutical Patent Law and Policy in Africa: A Survey of Selected SADC Member States', *Legal Studies*, 43(2): 331–350; See also T.A. Adekola (2020) 'Has the Doha Paragraph 6 System Reached Its Limits?', *Journal of Intellectual Property Law & Practice* 15(7), 525–529.

[70]See B. Sherman and L. Bently (1999) *The Making of Modern Intellectual Property Law* (Vol. 1). Cambridge University Press.

[71]See generally B. Mercurio (2018) *Drugs, Patents, and Policy: A Contextual Study of Hong Kong*. Cambridge University Press.

[72]See generally Article 27 of the TRIPS Agreement.

[73]See A. Taubman (2018) 'Climate Change and The Intellectual Property System: What Challenges, What Options, What Solutions?', www.wipo.int/export/sites/www/policy/en/climate_change/pdf/ip_climate.pdf (accessed 3 May 2023).

https://doi.org/10.1017/S147474562400020X Published online by Cambridge University Press

While these criteria are generally known in patent law, the key to an effective patent system is ensuring that issued patents conform to them in practice, which requires maintaining high standards of 'patent quality', From a South African standpoint, the absence of thorough patent examination creates opportunities for potential 'misuse'.[74] For instance, a major multinational company could file numerous patents in South Africa for a highly sought-after or groundbreaking technology without having to demonstrate to the South African Patent Office that these inventions deserve patent protection.[75] This failing of the domestic legislation could allow a tactic that could negatively affect the mRNA hub. Given that most of the recipient countries may lack substantial patent examination frameworks, they may consider outsourcing their examination processes in this regard.[76]

After a patent is granted for mRNA technologies, post-grant considerations become important as the technologies enter into a broader legal and regulatory environment. The focus should then shift toward how the patent owners can appropriately exercise their exclusive patent rights, and what remedies can be implemented to serve the public interest. Given that mRNA technologies are typically packaged together from several sources[77] and licensed through a range of arrangements and structures, regulators may scrutinize how a patent holder licenses technology, particularly for publicly funded or public sector institutions that hold key patents on valuable technologies which are of strong public interest. Post-grant questions that must be answered with regard to mRNA technologies for instance should include determining appropriate licensing structures and intellectual property management strategies to promote the dissemination of the technologies, establishing exceptions and limitations to patent law to safeguard the public interest, and interventions that override exclusive patent rights to address anticompetitive practices and other abuses of patent rights.

3.2 Patents, Technology Transfer, and the mRNA Hub

The role of patents in facilitating the transfer of technology is cardinal to attaining the objectives of the mRNA hub initiative. This role encompasses various aspects, such as international law, economics, policy context, innovation, competition policy, and ethical considerations.[78] Although the role is intricate, some general observations can be made when considering the mRNA technology transfer hub.

First, a mRNA technology patent does not inherently impede technology transfer. The success of technology transfer would depend on how the exclusive rights granted by a patent are utilized, the jurisdictions where the patent can be enforced, and how these rights are incorporated into suitable mechanisms for technology transfer. For instance, contrary to the notion that intellectual property impeded the transfer of mRNA vaccine technologies during the COVID-19 pandemic, what we actually saw was the critical role intellectual property played in facilitating voluntary licensing agreements and technology transfer for mRNA technologies. Several critical collaborations and partnerships that helped to end the pandemic would not have occurred without intellectual property protection. Lonza would not have partnered with Moderna to produce the active ingredient for Moderna's vaccine, Pfizer and BioNTech would not have collaborated, and Oxford

[74]C.B. Ncube (2021) 'South Africa's Three Decades of Access to Medicine Discourse: Blight or Benefit', *Intellectual Property Law and Access to Medicines*. Routledge, 235–251.

[75]C.B. Ncube (2014) 'The Draft National Intellectual Property Policy Proposals for Improving South Africa's Patent Registration System: A Review', *Journal of Intellectual Property Law & Practice* 9(10), 822–829.

[76]J. Phillips (2010) 'Outsourcing of IP Office Functions: No Longer a Joke', *Journal of Intellectual Property Law & Practice* 5(6), 389–389.

[77]X. Huang, N. Kong, X. Zhang, Y. Cao, R. Langer, and W. Tao (2022) 'The Landscape of mRNA Nanomedicine', *Nature Medicine*, 1–15.

[78]World Health Organization (2012) 'Local Production and Technology Transfer to Increase Access to Medical Devices: Addressing the Barriers and Challenges in Low-and Middle-Income Countries', https://apps.who.int/iris/bitstream/handle/10665/336774/9789241504546-eng.pdf.

https://doi.org/10.1017/S147474562400020X Published online by Cambridge University Press

University and AstraZeneca would not have engaged in manufacturing partnerships and licensing agreements in various regions including India.[79] These examples show that intellectual property does not inherently hinder technology transfer but rather that it could facilitate it.

Conversely, the absence of enforceable patent rights in a particular country does not automatically guarantee technology transfer. For example, least-developed countries are not obligated to protect patents under the TRIPS Agreement until 2034.[80] While the absence of patents in these jurisdictions should theoretically suggests that mRNA technologies can be exploited without fear of patent infringement, most least-developed countries often lack the infrastructure and technical know-how needed to reverse engineer patented technologies.[81] In this case, the problem shifts from the realm of intellectual property to non-intellectual property barriers to technology transfer, manufacturing, and access.

That being said, the transparency of the patent system, if effectively utilized, can facilitate technology transfer in the context of the mRNA hub. By monitoring technological advancements and trends, the patent system can track new players, geographical shifts, and the relative involvement of public and private sector entities.[82] Moreover, it can help prevent redundant research and development efforts, promote technological leapfrogging and cumulative development, and aid in structuring technology transfer agreements that incentivize the inclusion of improvements, know-how, and related technologies.[83]

While patents alone do not guarantee technology transfer, their effective utilization, in conjunction with transparent systems and appropriate strategies, can help enhance the mRNA hub's sustainability. In any case, the importance of know-how and ensuring the voluntary involvement of right holders in the technology transfer process is integral to the sustainability of the hub. In the course of research and development, vaccine developers accumulate considerable know-how necessary for vaccine manufacturing. Such know-how is usually not disclosed in patents or patent applications, related scientific publications or assessment reports of drug authorities. They are often transferred under non-disclosure agreements. Not getting the cooperation of the rights holders within the mRNA space would deprive the spokes of key manufacturing know-how for vaccine manufacturing. Hence, the imperative of rights holders cooperation is not just to ensure access to know-how but to also avoid intellectual property litigations.

Overall, the role of patents in technology transfer is intricate and multi-dimensional. It is important to dispel the assumption that obtaining a patent is a standalone method for technology transfer. Patents are employed in various ways to transfer technology based on the specific requirements of effective technology transfer. These methods include leveraging access to related technologies from different sources, promoting an open licensing structure, implementing cross-licensing arrangements, and bundling patented technology with non-patented elements such as manufacturing know-how, commercial information, or regulatory approval dossiers.[84] A synergetic consideration of these interrelated factors will help in charting a sustainable future for the mRNA hub and its spokes going forward.

[79]F. Addor (2023) 'How (Not) to Sleepwalk into the Next Pandemic!', *IIC-International Review of Intellectual Property and Competition Law*, 1–5.

[80]See, respectively, WTO 'Amendment of the TRIPS Agreement', Decision of 6 December 2005, www.wto.org/english/tratop_e/trips_e/wtl641_e.htm (last accessed 11 December 2022); WTO 'Extension of the transition period under Art 66.1 for least developed country members', WTO Doc IP/C/64, 12 June 2013, www.wto.org/english/tratop_e/trips_e/ta_docs_e/7_1_ipc64_e.pdf (last accessed 11 December 2022); WTO 'Extension of the transition period under Art 66.1 for least developed country members', WTO doc IP/C/88, 29 June 2021.

[81]S. Bhattacharya and S. Guriev (2006) 'Patents vs. Trade Secrets: Knowledge Licensing and Spillover', *Journal of the European Economic Association* 4(6), 1112–1147.

[82]K. Karachalios and S. Elahi (2009) 'Transparency, Trust, and the Patent System', *Journal of Intellectual Property Law & Practice*, 4(11), 809–814.

[83]Ibid.

[84]J.A. Cunningham, M. Menter, and C.Young (2017) 'A Review of Qualitative Case Methods Trends and Themes used in Technology Transfer Research', *The Journal of Technology Transfer* 42, 923–956.

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3.3 The Boundaries of Compulsory Licenses

The TRIPS Agreement permits the issuance of compulsory licenses under certain circumstances to allow third-party use of the patent without the authorization of the rights holder. This exception has been the subject of controversy since the inception of the TRIPS Agreement, and the exact contours of these exceptions have yet to be fully defined.[85] The various types of compulsory licenses are, for example, the third-party initiated compulsory license, government use compulsory license, compulsory license of related patents, and compulsory license for export of pharmaceuticals. For the mRNA hub-spoke model, if voluntary licensing fails and the parties cannot come to an agreement on reasonable licensing terms within a reasonable period, the legal option of compulsory licensing for dependent patents or third-party-initiated compulsory license may be considered.

As described in the previous section, the use of mRNA technologies often requires additional technologies such as delivery systems, which means that patent dependencies are likely to occur frequently. In cases where a later invention cannot be used without infringing an 'upstream' mRNA patent, the user would need to obtain a license from the relevant patent holder(s).[86] As a precondition for obtaining a compulsory license in a case of patent dependency, the TRIPS Agreement requires that the later invention constitutes 'an important technical advance of considerable economic significance in relation to the invention claimed in the first patent'.[87] Overall, the effectiveness of this type of compulsory license as an instrument of access does not appear straightforward, as it depends on several factors such as the interpretation of the standard for an important technical advance and the willingness of patent holders to grant voluntary licenses. While the lack of its practical use suggests that the provision may not have been applied in any jurisdiction, one might hypothesize that the very existence of the provision could be a factor contributing to the patent holders willingness to grant a voluntary license and engage in cross-licensing agreements. Platform technologies, such as mRNA technology, generally encourage dependent patent holders to collaborate and engage in voluntary cross-licensing.[88] Through the establishment of cross-licensing agreements for interdependent patents, companies can encourage collaboration, stimulate innovation, and facilitate growth for platform technologies. This approach ultimately leads to the expansion of market reach and returns, thereby reducing the necessity for compulsory licenses for interdependent patents.

In addition, as mRNA technology has great potential to address basic societal needs, such as public health, there is a possibility of implementing a compulsory license based on public interest, particularly in LMICs. However, the effectiveness of such a license would depend on how it is implemented under national law, the availability of local manufacturing technology, and the accessibility of technical know-how. As important as compulsory licenses may seem, they will usually not suffice without a comprehensive and effective transfer of know-how, which is essential to make use of patented technology. Accordingly, for 'medicinal products based on known

[85]B. Mercurio and D. Kim (2017) 'Introduction: A Holistic Approach to Pharmaceutical Patent Law and Policy', *Contemporary Issues in Pharmaceutical Patent Law*. Routledge, 1–6.

[86]A dependent invention refers to a situation where a patented invention cannot be exploited without infringing a patent with an earlier filing or priority date.

[87]See Article 31(l)i, ii, iii of the TRIPS Agreement states:

'(l) where such use is authorized to permit the exploitation of a patent ('the second patent') which cannot be exploited without infringing another patent ('the first patent'), the following additional conditions shall apply:

(i) The invention claimed in the second patent shall involve an important technical advance of considerable economic significance in relation to the invention claimed in the first patent;

(ii) the owner of the first patent shall be entitled to a cross-license on reasonable terms to use the invention claimed in the second patent; and

(iii) the use authorized in respect of the first patent shall be non-assignable except with the assignment of the second patent.'

[88]S. Arato and S. Kano (2021) 'Platform Technology Management of Biotechnology Companies in Japan', *Journal of Commercial Biotechnology* 26(3).

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methods, such as the use of small-molecule drugs or traditional vaccines using particles of a virus, a compulsory license may provide a ready-to-deploy mechanism for production and distribution'.[89] In contrast, in the case of mRNA-based vaccines, replicating the technical teaching underlying a patent 'without access to the related know-how is by no means trivial'.[90] This makes compulsory licenses less relevant to the production of mRNA-based vaccines.

Therefore, compulsory licensing cannot be viewed as an immediate solution due to its exceptional nature and case-by-case assessment.[91] These issues notwithstanding, in practice it is often the threat to issue a compulsory license (as opposed to the actual use) that serves an important purpose as it is a key bargaining chip for countries negotiating purchases from pharmaceutical companies.[92] The mRNA hub and spoke model could therefore increase the credibility of threats to issue a compulsory license by the spokes, serving as an effective instrument against which voluntary licenses may be negotiated. For this reason, and although imperfect, a compulsory license may play a supportive role in the wider effort to drive local production by the spokes through the mRNA hub.

3.4 Mitigating the Impact of Licensing Fees

Given the bourgeoning mRNA patent landscape, the impact of patent licensing fees on the price of vaccines and therapeutics manufactured by the hub can be significant. The payments that might have to be made and factored into the total cost of the manufactured products, could include an upfront 'technology access' license fee, milestone payments, and/or royalties calculated as a percentage of sales revenue. As such, spokes would need to ensure that the payments required in exchange for any license grant will not impact their ability to offer the final product at an affordable price for the final product. An option in this regard is the guideline provided in section 6.4 of the mRNA vaccine technology transfer agreement which states that:

> In the event that **[XXX]** is provided with access to Third Party IP for the purposes of research, development and/or commercialization of Product(s), **[XXX]** undertakes to use reasonable efforts to negotiate a licence to MPP for such Third Party IP under the same or similar terms as provided for in Section 6.3 herein[93]

Making a reasonable effort to negotiate a license to MPP will bring the technology into the pool for use by other spokes and the hub. Another option that could be considered is the possibility of negotiating lower royalty rates for sales or public sector purchases to help support a lower pricing strategy and the hub's goal of reducing the cost of vaccination.[94] While several studies provide a comprehensive overview of measures to disseminate mRNA technologies (compulsory licenses, waivers, etc.),[95] there remains a dearth of research on licensing practices in this field. In general,

[89]R. Hilty, P. Batista, S. Carls, D. Kim., M. Lamping, and P.R. Slowinski, (2021), 'Covid-19 and the Role of Intellectual Property: Position Statement of the Max Planck Institute for Innovation and Competition of 7 May 2021', Max Planck Institute for Innovation & Competition Research Paper, 13–21.

[90]Ibid.

[91]R. Hilty et al., supra n. 89.

[92]T.A. Adekola (2022) 'Compulsory Licenses in a Regional Context: An Appraisal of the TRIPS Amendment's Special Regional Treatment', *GRUR International* 71(9), 822–830.

[93]See Section 6.4 of the mRNA Technology Transfer Spoke Agreement Template, supra n. 25.

[94]F.M. Scherer and J. Watal (2002) 'Post-TRIPS Options for Access to Patented Medicines in Developing Nations', *Journal of International Economic Law* 5(4), 913–939.

[95]A. Kumar, J. Blum, T.T. Le, N. Havelange, D. Magini, and I.K. Yoon (2022) 'The mRNA Vaccine Development Landscape for Infectious Diseases', *Nature Reviews Drug Discovery* 21(5), 333–334; S. Thambisetty, A. McMahon, L. McDonagh, H.Y. Kang, and G. Dutfield (2022) 'Addressing Vaccine Inequity During the Covid-19 Pandemic: The Trips Intellectual Property Waiver Proposal And Beyond', *The Cambridge Law Journal* 81(2), 384–416; J. Baachus (2020) 'An Unnecessary Proposal: A WTO Waiver of Intellectual Property Rights for COVID-19 Vaccines', *Cato Institute, Free Trade Bulletin*, (78).

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one could project that licensing practices within the complex mRNA space would be unfavourable to the mRNA hub's business environment and potentially could demotivate the spokes. Therefore, more comprehensive research on the functioning of access to mRNA technologies, through voluntary contracts in the context of the mRNA hub I,s necessary.

4. Recommendations

4.1 Regional Coordination

Several key regional strategic activities would have to be prioritized in order to achieve the objectives set forth by the mRNA Technology Transfer Hub. First, is the need for the harmonization of regulatory standards and processes across countries to be supplied by the spokes. This alignment would reduce unnecessary barriers and ensure consistent quality control, safety standards, and regulatory compliance when distributing mRNA-based vaccines or therapeutics across borders.[96] Another critical aspect is the need to harmonize the public health-related TRIPS flexibilities within the national laws of the spoke and their regional target markets. This would involve incorporating provisions that safeguard public health interests and promote access to affordable medicines.[97]

For instance, Article 27 of the TRIPS Agreement provides ample room for Members to tailor their laws to meet specific needs and objectives and provide the meaning and scope of each of the criteria for patentability. The recommended approach for the spoke countries is to embrace strict rules that fully respect prevailing international standards (including the granting of second medical use patents) but could also guard against over-protection and interests that run counter to those of the goals of the mRNA hub.[98] Clear guidelines on the definition of patentability criteria in a manner that extends protection to genuine innovations only while also rewarding R&D investments should be put in place.[99]

For a compulsory license, as noted in the previous section, it is the threat of its use that would be a valuable bargaining chip for extracting concessions from the rights holder in the context of the mRNA hub.[100] Hence, spoke countries should have compulsory license provisions in place in order to be in a better position to threaten its use when such need arises. An example is to provide that a compulsory licence may be issued if the invention, though capable of being worked in the country, is not being worked on a commercial scale and there is no satisfactory reason for non-working. The legality of local working requirements – domestic provisions that allow the grant of a compulsory licence when a patent is not 'worked' in that country – are questionable under Article 27 of the TRIPS Agreement, which prohibits discrimination as to 'whether products are imported or locally produced'.[101] However, the consistency of the provision has never been tested in dispute settlement, and there is no evidence that WTO Members maintaining local working requirements are concerned about any inconsistency with the TRIPS Agreement.[102]

[96]See O.A. Olatunji (2023) 'Between Regional Recommendations and National Implementation: An Analysis of the East African Community Partner States' Legislative Responses to TRIPS Obligations', *IIC-International Review of Intellectual Property and Competition Law*, 1–37.

[97]T.A. Adekola (2020) 'Regional Mechanism Under Doha Paragraph 6 System-The Largely Untested Alternative Route for Access to Patented Medicines', *Asian Journal of WTO & International Health Law and Policy* 15, 61.

[98]B. Mercurio, T.A. Adekola, and C.F. Tsega (2023) 'Pharmaceutical Patent Law and Policy in Africa: A Survey of Selected SADC Member States', *Legal Studies*, 1–20.

[99]Ibid.

[100]Ibid.

[101]B. Mercurio and M. Tyagi (2010) 'Treaty Interpretation in WTO Dispute Settlement: The Outstanding Question of the Legality of Local Working Requirements', *Minnesota Journal of International Law* 19, 326 (arguing that Art 31 of the Vienna Convention on the Law of Treaties together with the provisions in the TRIPS Agreement and Doha Declaration and the principles of good faith domestic legislation local working requirements do not unjustifiably discriminate against other members in violation of Art 27 of the TRIPS Agreement).

[102]Ibid.

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For parallel importation, an unrestricted international exhaustion regime is highly recommended. Hence, patent laws must be clear and unequivocal in this regard. International exhaustion can benefit by helping facilitate the importation of patented products from the cheapest market in order to assist in meeting prevailing health needs.[103] As simple as this recommendation is, the parallel importation of pharmaceuticals is controversial and complex. spokes must be mindful of other issues beyond trade, including health policies, consumer protection, and medical regulations.[104] National marketing approval for pharmaceutical products, labelling laws, import authorizations, and other formalities make use an unrestricted regime even more complicated in practice. [105] The ecosystem of parallel trade in pharmaceuticals is beyond the scope of this paper, but from an intellectual property perspective, the international exhaustion regime is a viable way to facilitate access to pharmaceuticals for low-income countries. Overall, there would be a need to establish a regionally streamlined approach to patent protection in a manner that ensures that mRNA technology developers receive a consistent scope of patent rights across the hub's network.[106]

4.2 Fulfilling Developed Countries' Obligations under TRIPS

During the negotiations leading to the adoption of the TRIPS Agreement, less developed countries were reluctant to adopt and embed in their national intellectual property laws the minimum standards established by the international agreement.[107] This reservation is borne out of two factors. First, as less developed countries lack the technological infrastructure needed for groundbreaking inventions, they saw no reason to offer protection to such innovations. Second, offering such minimum protection would preclude them from (in theory) enjoying the myriad of opportunities, which come with a lax, laissez-faire regime such as technology transfer and local technological development. Negotiations were complicated and difficult, but ultimately less developed countries agreed to incorporate intellectual property into the multilateral trading system in exchange for several trade concessions, most notably in the form of enhanced agricultural access to developed country markets. That being said, less developed countries were successful in negotiating for the inclusion of most of the provisions of the so-called 'B Text' and embedding flexibilities in the agreement.[108]

One such concession is Articles 67 and 66.2 of TRIPS Agreement.[109] Article 66.2 stipulates that high-income countries 'shall provide incentives to enterprises and institutions in their territories for the purpose of promoting and encouraging technology transfer to least-developed country Members in order to enable them to create a sound and viable technological base.'[110] Article 67 deals essentially with the obligation of developed countries to facilitate the preparation of laws and regulations that are TRIPS-compliant, establish or restructure national intellectual

[103]B. Mercurio, T.A. Adekola, and C.F. Tsega (2023) 'Pharmaceutical Patent Law and Policy in Africa: A Survey of Selected SADC Member States', *Legal Studies* 1–20.

[104]Ibid.

[105]Ibid.

[106]Ibid.

[107]P.K. Yu (2009) 'The Objectives and Principles of the TRIPS Agreement', *Houston Law Review* 46, 797–1046, at 798–800.

[108]D.J. Gervais (2005) 'Intellectual Property, Trade and Development: The State of Play', *Fordham Law Review* 74(2), 505–535, at 507–508

[109]'The provision of Article 66.2 was reinforced in Paragraph 7 of the Doha Declaration on TRIPS and Public Health where the WTO Ministers reaffirmed … the commitment of developed-country members to provide incentives to their enterprises and institutions to promote and encourage technology transfer to least-developed country members pursuant to Article 66.2. The WTO Ministerial Conference has confirmed that Article 66.2 is not merely a directory but mandatory. This is evident in the Decision on Implementation-Related Issues and Concerns adopted in Doha on 14 November 2001. Subparagraph 112 of the Decision on Implementation states: Reaffirming that the provisions of Article 66.2 of the TRIPS Agreement are mandatory, it is agreed that the TRIPS Council shall put in place a mechanism for ensuring the monitoring and full implementation of the obligations in question.'

[110]See Article 66.2 of TRIPS Agreement.

https://doi.org/10.1017/S147474562400020X Published online by Cambridge University Press

property offices, provide financial assistance, and train personnel. While Article 67 does not mention the international transfer of technology, its scope is arguably wide enough to cover the means of making Article 66 effective.

However, since TRIPS came into force nearly three decades ago, the implementation of these provisions has remained quite nebulous and controversial.[111] The first challenge with Article 66.2 has been that the developed country's obligation ends with providing incentives. There is no obligation to intervene directly in the transfer of technology. Their role is no more than encouraging private holders of to engage in business partnerships with local firms in developing countries. Gervais noted that the ability of developed state governments to foster technology transfer is usually limited by two factors: that governments do not own the vast majority of the available technologies; and that they cannot compel the private sector to transfer the technologies.[112] Thus, the incentives provided by developed country governments can only serve the purpose of promoting, encouraging, and facilitating technology transfer projects in least-developed countries.

The second challenge is the lack of clarity regarding how the obligations should be fulfilled and to what end. The letter of the law has been said to offer scant guidance on questions such as how many incentives, and how much technology transfer is enough? From how many developed countries to how many LDCs? For how long? Who decides?

The mRNA hub may present a viable opportunity to bring some clarity to these obligations. With the mRNA hub, the provisions of Articles 66.2 and 67 may have taken a distinct character and there should no longer be any ambiguity or lack of clarity as the mRNA hub mirrors what the negotiators of the TRIPS agreement must have envisaged during TRIPS negotiations. If developed countries were to endorse the efforts of the hub (as seems to be the case), they could offer financial support in the form of grants, subsidies, and tax benefits to pharmaceutical companies that collaborate with mRNA hub. By doing so, these countries would be fulfilling their obligations to facilitate the development of a sustainable technological foundation in least-developed countries as outlined in Article 66.2 of the TRIPS Agreement.[113] Of particular significance in this context is the potential for the governments representing the holders of patents to be willing to make patented technology accessible through buy-outs, patent pools, or geographically segmented licensing arrangements while also providing financial support.

Furthermore, the ongoing negotiations for the WHO pandemic treaty may present a significant opportunity to reinforce the fundamental objectives and principles of the TRIPS Agreement within the international community and to implement them for a more equitable management and sharing of intellectual property and know-how necessary for pandemic preparedness and response.[114] While there are concerns regarding whether and to what extent the treaty would be legally binding and/or have a strong enforcement mechanisms,[115] its primary objective aligns with that of the mRNA hub – promoting a comprehensive approach to enhancing national, regional, and global capacities and resilience against future pandemics.[116] If effectively leveraged,

[111]See A. Subramanian and J. Watal (2000) 'Can Trips serve as an Enforcement Device for Developing Countries in the WTO?', *Journal of International Economic Law* 3(3), 403–416 see also J. Watal and L. Caminero (2019) '*Least-Developed Countries, Transfer of Technology and the TRIPS Agreement*. Springer Singapore, 199–228.

[112]D. Gervais (2014) 'TRIPS and Development', *The Sage Handbook of Intellectual Property*. Los Angeles/London: Sage, 95–112.

[113]Article 66.2 of the TRIPS agreement states that: 'Developed country Members shall provide incentives to enterprises and institutions in their territories for the purpose of promoting and encouraging technology transfer to least-developed country Members in order to enable them to create a sound and viable technological base.'

[114]See Proposal for negotiating text of the WHO Pandemic Agreement, Revised draft of the negotiating text of the WHO Pandemic Agreement (accessed 18 February 2024).

[115]N.A. Evaborhene, J.O. Oga, O.V. Nneli, and S. Mburu (2023). 'The WHO Pandemic Treaty: Where are We on Our Scepticism?', *BMJ Global Health* 8(6) e012636.

[116]K. Perehudoff, E.T. Hoen, K. Mara, T. Balasubramaniam, F. Abbott, B. Baker, and J. Love (2022). 'A pandemic Treaty for Equitable Global Access to Medical Countermeasures: Seven Recommendations for Sharing Intellectual Property, Know-How and Technology', *BMJ Global Health*, 7(7), e009709.

https://doi.org/10.1017/S147474562400020X Published online by Cambridge University Press

the treaty could offer a fresh opportunity to put technology transfer and the sharing of intellectual property at the heart of global pandemic preparedness.

5. Conclusion

While the idea of local production in LMICs is not new, the hurdles have always proven to be too high to take the idea further. However, the pandemic has demonstrated significant trade disruptions, prompting a change in perspective and necessitating a reevaluation of trade patterns and the overall pharmaceutical production framework. While the model of the mRNA technology transfer hub examined in this article looks promising, it is essential that advocates and strategists strategically navigate the potential intellectual property hurdles in order to avoid unnecessary and expensive errors that could jeopardize the long-term viability of local production. While several questions remain open-ended regarding the mRNA hub-spoke model, the most sustainable path is to guarantee the support and cooperation of the big biotech companies with patent rights on mRNA 'commons'. This will help to avoid intellectual property litigations, ensure smooth technology diffusion to and within the spokes, and foster better preparedness for future public health emergencies.

In the absence of such cooperation, the hub and the spokes will have to fall back on available options existing within the TRIPS Agreement. The TRIPS Agreement incorporates safeguards that seek to ensure a balance between the rights and obligations of inventors and users. Even though the TRIPS Agreement prescribes uniform minimum standards, in principle, it is for the respective WTO members to determine the forms of protection deemed appropriate to achieve – or to avoid – effects that are considered (un)desirable for public health reasons. The best approach would be to ensure that the spoke countries and countries within their region of supply frame their pharmaceutical patent laws and policies to take full advantage of the flexibilities existing within the TRIPS Agreement. Although NGOs and certain scholars assert that the TRIPS flexibilities are too complicated to use, the fact that Afrigen could rely on Article 30 of TRIPS to reverse engineer Moderna's vaccine has shown that these flexibilities can work and are in fact an integral part of efforts to drive access to pharmaceuticals. Other flexibilities remain underutilized in most LMICs.

What is clear is that the pandemic has served as a disruption to the pharmaceutical sector and the production and distribution of vaccines and medicines. Similar to other goods, manufacturing in the pharmaceutical sector is no longer simply about efficiencies and comparative advantage. Instead, thinking, strategies, and priorities have shifted, and diversified local production is now seen as a necessary risk management strategy that can better guard against supply chain disruption and ensure more equitable access to vaccines. This, in turn, implicates supply and license agreements, and thus IPRs. The systemic change brings hope for strengthened resilience and longer-term sustainability, but also several immediate challenges. This article sought to address of the challenges relating to intellectual property and call upon others to raise awareness of further challenges that must be addressed to provide a better chance of success for the hub and spoke mRNA vaccine production model and more equitable pharmaceutical sector in the future.

Acknowledgement. This research is supported by the Hong Kong RGC Senior Research Fellow Scheme 2022/23 for a project entitled: Access to Vaccines in a Post-COVID-19 World: Sustainable Legal and Policy Options (Project No. SRFS2223-4H01). The views expressed in this publication do not necessarily represent the views of others involved in the project.

Cite this article: Adekola TA, Mercurio B (2025). mRNA Technology Transfer Hub and Intellectual Property: Towards a more Equitable and Sustainable Model. *World Trade Review* **24**, 302–320. https://doi.org/10.1017/S147474562400020X