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INNOVATION AND PATENTING ACTIVITIES OF COVID-19 VACCINES IN WTO MEMBERS: ANALYTICAL REVIEW OF MEDICINES PATENT POOL (MPP) COVID-19 VACCINES PATENT LANDSCAPE (VAXPAL)

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World Trade Organization

Manuscript date: 18 January 2022

Disclaimer: This is a working paper, and hence represents research in progress. This paper represents the opinions of the authors and is the product of professional research. It is not meant to represent the positions or opinions of the WTO or its Members, nor the official positions of any staff members. Any errors are attributable to the authors.

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ABSTRACT

This working paper provides a statistical analysis of 74 patent families which cover subject matter relevant to ten COVID-19 vaccines. These vaccines have accounted for 99% of the global COVID-19 vaccine production as of 31 December 2021, comprising over ten billion doses. Eight of them, namely BNT162b2 (Pfizer/BioNTech), AZD1222 (AstraZeneca/Oxford), Ad26.COV2-S (J&J), mRNA-1273 (Moderna), BBIBP-CorV (Sinopharm/Beijing), Coronavac (Sinovac), Covaxin (Bharat/ICMR), and NVX-CoV2373 (Novavax), have been approved by the World Health Organization (WHO) for inclusion in its Emergency Use Listing (EUL). The analysis is based on VaxPaL, a COVID-19 vaccines patent database developed by the Medicines Patent Pool (MPP). Through the detailed examination of patent applicants, filing dates, and offices of first and subsequent filing, the paper identifies patterns and trends of innovation and patenting activities of COVID-19 vaccines in WTO Members, and presents the legal status of the 74 patent families in 105 jurisdictions. This information may provide useful background for policymakers on the significance and potential impact of these patent families with relevance to the access to and production of these vaccines in their individual countries. This, in turn, may help support practical assessments as to potential options within and beyond the current TRIPS framework to promote equitable access to COVID-19 vaccines.

Keywords: COVID-19, vaccine, patent, whole virus, viral vector, protein subunit, mRNA, filing dates, office of first filing, office of subsequent filing, legal status

JEL classifications: K11, K15, K30, O30, O31, O34, I18

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Table of Contents

EXECUTIVE SUMMARY 5
1 BACKGROUND 7
2 OBJECTIVES 9
3 MPP VAXPAL – DATA COLLECTION AND SEARCH METHODLOGY 10
3.1 Vaccine selection 11
3.2 Patent data collection and search methodology 12
3.3 Information in VaxPaL 12
4 OVERVIEW OF TEN COVID-19 VACCINES: TECHNOLOGY PLATFORMS AND CURRENT MANUFACTURING 13
4.1 Overview of four technology platforms for COVID-19 vaccine development 13
4.2 Current manufacturing of COVID-19 vaccines based on four technology platforms 16
5 INNOVATION AND PATENTING ACTIVITIES OF COVID-19 VACCINES 17
5.1 Innovation and patenting activity by vaccine technology platform 17
5.2 Patenting activity by nature of patent applicant 20
5.3 Patenting activity by patent first filing date 23
5.4 Patenting activity by office of first filing (OFF) 26
5.5 Patenting activity by office of subsequent filing (OSF) 29
5.6 Legal status of patent families by jurisdiction 32
6 KEY FINDINGS 36
BIBLIOGRAPHY 38

EXECUTIVE SUMMARY

This working paper provides a statistical analysis of 74 patent families which cover subject matter relevant to ten COVID-19 vaccines. These ten vaccines, comprising over ten billion doses, have accounted for 99% of the global COVID-19 vaccine production as of 31 December 2021. Eight of them, namely BNT162b2 (Pfizer/BioNTech), AZD1222 (AstraZeneca/Oxford), Ad26.COV2-S (J&J), mRNA-1273 (Moderna), BBIBP-CorV (Sinopharm/Beijing), Coronavac (Sinovac), Covaxin (Bharat/ICMR), and NVX-CoV2373 (Novavax), have been approved by the World Health Organization (WHO) for inclusion in its Emergency Use Listing (EUL).

The statistical analysis is based on VaxPaL, a COVID-19 vaccines patent database released by the Medicines Patent Pool (MPP) on 9 June 2021. The paper introduces the ten COVID-19 vaccines covered by the VaxPaL data, the four types of technology platforms used in their development, as well as their current global production status.

Through an analytical review of the VaxPaL data, the paper describes patterns and trends of innovation and patenting activities related to the ten COVID-19 vaccines, including what has been patented, who has applied for these patents, when and where these patents have been filed, and the legal status of the 74 patent families in various jurisdictions. Several key findings can be summarized as follows:

- There are wide variations in the number of patent families involved in each COVID-19 vaccine, reflecting the different technology platforms deployed for their development. In general, mRNA and viral vector-based vaccines are more patent-intensive than whole virus and protein subunit-based vaccines. Nevertheless, there is different patent intensiveness even between the vaccines based on the same technology platform.

- The review of patenting trends highlights a major role on the part of private enterprises in COVID-19 vaccine innovation and development, while suggesting that public research institutions and universities have largely made their contributions through conducting basic scientific research. Among these private enterprises, it is SME biotech companies rather than traditional large vaccine companies that have made the most substantive contributions to COVID-19 vaccine development, particularly in the early development stages.

- Patenting activities of the 74 patent families spread from 1996 to 2021, and most patent applications were filed before December 2019. The successful development of COVID-19 vaccines benefits from years of medical research and development before and after the outbreak of the COVID-19 pandemic.

- Of the 74 patent families, a large majority are based on applications first filed in the United States or Europe. Analysis of these patent families indicates that COVID-19 vaccine innovation activities, particularly mRNA-related innovation, mainly took place in the United States and Europe, consistent with their relative technical strengths in the pharmaceutical and biotechnology industries. Meanwhile, the great majority of the 74 patent families have subsequent patent filings in other jurisdictions, mainly including Canada; Australia; Japan; China; India; Republic of Korea; Singapore; Israel; Mexico; New Zealand; Hong Kong, China; Brazil; Russian Federation; EAPO member states; and South Africa. Most of the countries receiving first or subsequent patent filings are among top 25 innovation economies indicated in the World Intellectual Property Organization (WIPO) Global Innovation Index 2021.

- The legal status of the 74 patent families involved in the ten COVID-19 vaccines is highly divergent across different jurisdictions. A majority of patents, mainly related to mRNA and viral vector-related technologies, have been granted in the United States, Australia, EPO member states, Japan, Russian Federation, China, Canada, South Africa, New Zealand, Israel, and Republic of Korea. In most developing countries, the information on whether patent applications for these 74 patent families have been made or not remains unavailable.

Thus, there is no such thing as an "international patent" or "COVID-19 vaccine patent", nor a one-on-one correspondence between any current vaccine and one specific patent. Country-level analysis of the legal status of these 74 patent families is ultimately essential for national policy and decision makers to make evidence-based holistic national and regional policies in order to promote technology transfer and strengthen local production capacity. A clear understanding of the legal status of

patents and patent applications in distinct jurisdictions is also crucial to inform the ongoing policy debate on the role of IP rights in the promotion of technology transfer and local production. It may contribute to identifying potential IP-related obstacles to local production, to developing corresponding IP strategies to address any identified obstacles, and more broadly, to making well-informed technology and public health policies and legislative decisions in response to the COVID-19 crisis and future pandemics.

1 BACKGROUND

Since its outbreak in January 2020, the COVID-19 pandemic has caused approximately 285 million confirmed infection cases and over 5 million deaths globally.[1] At the time of writing, there is still few effective medical treatments for COVID-19.[2] Universal vaccination is considered as a critical part of the solution to end this pandemic. With unprecedented speed, more than 300 vaccine candidates have been developed and tested at pre-clinical or clinical stages, among which eight have been evaluated and approved for inclusion in the WHO Emergency Use Listing (EUL) since December 2020.[3]

In the meantime, vaccine manufacturers have reportedly produced 1.5 billion doses per month, and, as of 31 December 2021, the total manufacturing output has surpassed the 10.9 billion dose mark.[4] According to one estimate, by June 2022, total vaccine production will reach 24 billion which may outstrip global demand.[5]

Despite these impressive achievements in vaccine research and development (R&D) and production, there are still many challenges in the global fight against COVID-19, notably equitable and universal distribution of COVID-19 vaccines. By the end of 2021, while 58% of the world's population has received at least one dose of a COVID-19 vaccine and 49% has been fully vaccinated by the time of writing, there is a sharp uneven rollout of vaccines between high-income and low- and middle-income countries (LMICs).[6]

Uneven distribution of and access to vaccines is not only a main obstacle to containing the pandemic and to supporting global economic recovery, but is also morally unacceptable. As Dr Tedros Adhanom Ghebreyesus, Director-General of the WHO, has said, "[e]conomically, epidemiologically and morally, it is in all countries' best interest to use the latest available data to make lifesaving vaccines available to all."[7]

There are many root causes for today's uneven distribution of vaccines, including unbalanced distribution of global vaccine manufacturing capacities, disruptions to global supply chains, lack of regulatory coherence, and a large number of advance purchase agreements between high-income countries and vaccine producers.[8] Promoting technology transfer and local production is one of the measures that governments, particularly of LMICs, seek to deploy in order to improve affordable and more equitable access to COVID-19 vaccines.

In March 2020, realizing the importance of equitable global access to COVID-19 health technologies, the WHO made the Solidarity Call to Action, which, *inter alia*, calls on governments to facilitate open sharing of knowledge, intellectual property (IP) and data necessary for COVID-19 related health

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[1] WHO, 'Timeline: WHO's COVID-19 Response' <www.who.int/emergencies/diseases/novel-coronavirus2019/interactive-timeline> accessed 12 January 2022.

[2] At the time of writing this paper, Merck and Pfizer are developing their respective COVID-19 oral antiviral treatment candidates, molnupiravir (MK-4482 and EIDD-2801) and ritonavir (PF-07321332). The MPP has signed licensing agreements with both companies in October 2021. MPP, 'The Medicines Patent Pool (MPP) and MSD enter into licence agreement for molnupiravir, an investigational oral antiviral COVID-19 medicine, to increase broad access in low- and middle- income countries' (27 October 2021) <https://medicinespatentpool.org/news-publications-post/mpp-msd-new-licence-announcement-molnupiravir>; MPP, 'Pfizer and The Medicines Patent Pool (MPP) Sign Licensing Agreement for COVID-19 Oral Antiviral Treatment Candidate to Expand Access in Low- and Middle-Income Countries' (16 November 2021) < https://medicinespatentpool.org/news-publications-post/pfizer-and-the-medicines-patent-pool-mpp-sign-licensing-agreement-for-covid-19-oral-antiviral-treatment-candidate-to-expand-access-in-low-and-middle-income-countries> accessed 24 November 2021.

[3] WHO, 'Status of COVID-19 Vaccines within WHO EUL/PQ evaluation process, 23 December 2021' <https://extranet.who.int/pqweb/sites/default/files/documents/Status_COVID_VAX_23Dec2021.pdf> accessed 13 January 2022.

[4] Airfinity, 'COVID-19' <www.airfinity.com/areas/covid-19> accessed 12 January 2022.

[5] ibid.

[6] Our World in Data, 'Coronavirus (COVID-19) Vaccinations' <https://ourworldindata.org/covid-vaccinations> accessed 12 January 2022.

[7] WHO, 'Vaccine inequity undermining global economic recovery' (22 July 2021) <www.who.int/news/item/22-07-2021-vaccine-inequity-undermining-global-economic-recovery> accessed 13 October 2021.

[8] Helen Lock, 'Vaccine Nationalism, Everything You Need to Know' (*Global Citizen*, 11 February 2021) <www.globalcitizen.org/en/content/what-is-vaccine-nationalism/> accessed 28 September 2021.

products through national legal and policy measures.[9] It also calls on holders of knowledge, IP, and data to voluntarily share, license, or not to enforce such rights during the COVID-19 pandemic, so as to facilitate the widescale production, distribution, sale, and use of such health technologies throughout the world.

At the 74th World Health Assembly in May 2021, WHO Member States adopted a resolution on strengthening local production of medicines and other health technologies in order to improve access. The resolution urges Member States, *inter alia*, to develop evidence-based holistic national and regional policies to strengthen the local production of quality, safe, effective, and affordable health technologies.[10] It also urges WHO Members to take into account the rights and obligations in the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement[11]), including those affirmed by the Doha Declaration on the TRIPS Agreement and Public Health[12], in order to promote access to medicines.

In parallel to the aforementioned WHO process, governments, civil society organizations and other stakeholders have been engaged in a heated debate on a longstanding public policy issue, that is, the role for IP protection, particularly patent protection, in the promotion of technology transfer and local production. More specifically, the debate focuses on whether the current international legal framework for the protection of IP rights, mainly established by the WTO TRIPS Agreement, provides an adequate framework for WTO Members to promote technology transfer and local production, and whether the flexibilities contained in the TRIPS Agreement can be implemented effectively in practice by WTO Members to address the current issue of vaccine access.

This policy debate was brought to the WTO Council for Trade-Related Aspects of Intellectual Property Rights (TRIPS Council) by India and South Africa in October 2020 through submitting a proposal suggesting a waiver for all WTO Members on the implementation of certain provisions of the TRIPS Agreement, including patent provisions, in relation to the prevention, containment or treatment of COVID-19 (TRIPS waiver proposal).[13] According to the proponents, the objective of the TRIPS waiver proposal is to avoid barriers to the timely access to affordable vaccines and medicines or to scaling-up of research, development, manufacturing, and supply of essential medical products.[14] On the other hand, in June 2021, the European Union made its own submission calling for Members to discuss how to facilitate the use of existing compulsory licensing provisions in the TRIPS Agreement, namely Articles 31 and 31*bis*, to accelerate vaccine production and equitable global distribution.[15] In their view, there is no concrete indication that IP rights have been a genuine barrier to accessing COVID-19 related vaccines and medicines, and that IP rights are only one aspect of many that affect their manufacture and distribution.[16]

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[9] WHO, 'Solidarity Call to Action' <www.who.int/initiatives/covid-19-technology-access-pool/solidarity-call-to-action> accessed 28 September 2021.

[10] WHO, 'Strengthening local production of medicines and other health technologies to improve access' (25 May 2021) 74/A/CONF./1.

[11] Agreement on Trade-Related Aspects of Intellectual Property Rights (15 April 1992) LT/UR/A-1C/IP/1 <www.wto.org/english/docs_e/legal_e/27-trips_01_e.htm>.

[12] WTO, 'Doha Declaration on the TRIPS Agreement and Public Health' (14 November 2001) WT/MIN(01)/DEC/2 <www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.htm>.

[13] WTO, 'Waiver from Certain Provisions of the TRIPS Agreement for the Prevention, Containment and Treatment of COVID-19: Communication from India and South Africa' (2 October 2020) IP/C/W/669, Add.1-16. Since October 2020, the proposal has been co-sponsored by the African Group, the Plurinational State of Bolivia, Egypt, Eswatini, Fiji, India, Indonesia, Jordan, Kenya, the Least-Developed Countries (LDC) Group, Maldives, Mozambique, Mongolia, Namibia, Pakistan, South Africa, Vanuatu, the Bolivarian Republic of Venezuela, and Zimbabwe. After eight months' discussion on the proposal in the TRIPS Council's formal and informal meetings, the co-sponsors submitted a revised proposal to reconcile various positions in May 2021. The revised proposal was also sponsored by Malaysia and Argentina. WTO, 'Waiver from Certain Provisions of the TRIPS Agreement for the Prevention, Containment and Treatment of COVID-19: Revised Decision Text' (25 May 2021) IP/C/W/669/Rev.1, Add.1–3.

[14] WTO, 'Minutes of the Meeting of Council for Trade-Related Aspects of Intellectual Property Rights' Item on Proposal for a Waiver from Certain Provisions of the TRIPS Agreement for the Prevention, Containment and Treatment of COVID-19 (14 December 2020 - 6 January 2022) IP/C/M/96 - IP/C/M/103, IP/C/M/96/Add.1 - IP/C/M/103/Add.1.

[15] WTO, 'Urgent Trade Policy Responses to the COVID-19 Crisis: Intellectual Property' (4 June 2021) IP/C/W/680. As a follow-up, the European Union submitted its proposal for a draft text on Declaration on the TRIPS Agreement and Public Health in the Circumstances of a Pandemic on 18 June 2021. WTO, 'Declaration on the TRIPS Agreement and Public Health in the Circumstances of a Pandemic' (18 June 2021) IP/C/W/681.

[16] WTO (n 14).

Since October 2020, WTO Members have been engaged in inclusive and comprehensive discussions on the TRIPS waiver proposal, but still have different perspectives on the appropriate role for IP protection, particularly patent protection, to play in ramping up global manufacturing capacity and promoting local production.[17] In the meantime, through organizing and participating in a series of events on the issue of COVID-19 and vaccines equity, the WTO has been working with other international organizations, key Members, and leading vaccine manufacturers to better understand the challenges preventing the production, scaling up, and distribution of vaccines.[18] Notably, in June 2021, the Directors General of the WHO, the WIPO, and the WTO, agreed to strengthen their support to Members battling the pandemic by collaborating on a series of workshops to augment the flow of information on the pandemic and by implementing a joint platform for tripartite technical assistance to Members relating to their needs for medical technologies.[19] In the meantime, the WTO also urged its Members to find pragmatic compromises in their ongoing negotiations on the TRIPS waiver proposal.[20]

2 OBJECTIVES

The role of IP rights in the promotion of technology transfer and local production in the area of public health has been widely discussed in the international IP community for many years.[21] It is commonly understood that technology transfer and local production depend on many conditions, and IP protection is only one of these conditions which in itself will not be decisive.[22] Nevertheless, a sound IP system can be used and designed to create an enabling environment for technology transfer and local manufacturing.

As mentioned above, the TRIPS Agreement provides an international legal framework for the protection of IP rights, and provides considerable flexibilities for WTO Members to design such a sound IP system at the domestic level. In 2010, in the context of the discussions on the WIPO Development Agenda, the WIPO Secretariat prepared a report on the issue of patent-related flexibilities in the TRIPS Agreement and their legislative implementation at the national and regional level.[23] In the report, a non-exhaustive list of patent flexibilities is grouped in three categories according to the status of patent application or the point in time at which Members may resort to them: flexibilities in the process of acquisition of the patent right; flexibilities related to the scope of

[17] ibid.

[18] WTO, 'International organizations discuss how to improve access to COVID vaccines, countermeasures' (22 December 2021) <www.wto.org/english/news_e/news21_e/covid_22dec21_e.htm>; WTO, 'International organizations, vaccine manufacturers agree to intensify cooperation to deliver COVID-19 vaccines' (16 September 2021) <www.wto.org/english/news_e/news21_e/covid_16sep21_e.htm>; WTO, 'High-Level Dialogue on "Expanding COVID-19 vaccine manufacture to promote equitable access" - Remarks by DG Okonjo-Iweala' (21 July 2021) <www.wto.org/english/news_e/spno_e/spno12_e.htm>; WTO, 'WHO-WTO dialogue steps up efforts for increased COVID-19 vaccine production and equitable access' (21 July 2021) <www.wto.org/english/news_e/news21_e/igo_21jul21_e.htm>; WTO, 'DG Okonjo-Iweala calls on WTO members to tackle vaccine inequity' (21 May 2021) <www.wto.org/english/news_e/news21_e/dgno_21may21_e.htm>; WTO, 'Statement of Director-General Ngozi Okonjo-Iweala on USTR Tai's statement on the TRIPS waiver' (6 May 2021) <www.wto.org/english/news_e/news21_e/dgno_06may21_e.htm>; WTO, 'DG Okonjo-Iweala underlines urgent need to address equitable access to vaccines' (5 May 2021) <www.wto.org/english/news_e/news21_e/gc_05may21_e.htm>; WTO, 'DG Okonjo-Iweala calls for follow-up action after WTO vaccine equity event' (14 April 2021) <www.wto.org/english/news_e/news21_e/dgno_14apr21_e.htm>; WTO, 'Chair Summary following "COVID-19 and Vaccine Equity: What Can the WTO Contribute?"' (14 April 2021) <www.wto.org/english/news_e/spno_e/spno7_e.htm> accessed 12 January 2022.

[19] WTO, 'WHO, WIPO, WTO map out further collaboration to tackle COVID-19 pandemic' (23 June 2021) <www.wto.org/english/news_e/news21_e/igo_23jun21_e.htm> accessed 18 January 2022.

[20] WTO, 'Members discuss contours of potential MC12 deliverables' (3 May 2021) <www.wto.org/english/news_e/news21_e/hod_03may21_e.htm> accessed 12 January 2022.

[21] WIPO, 'Study on the Role of Patent Systems in Promoting Innovative Medicines, and in Fostering the Technology Transfer Necessary to Make Generic and Patented Medicines Available in Developing Countries and Least Developed Countries' (10 October 2014) SCP/21/8; WHO, *The Role of Intellectual Property in Local Production in Developing Countries: Opportunities and Challenges* (WHO 2016) <https://apps.who.int/iris/handle/10665/336683>.

[22] WHO, *Local Production and Technology Transfer to Increase Access to Medical Devices: Addressing the barriers and challenges in low- and middle-income countries* (WHO 2012) <www.who.int/medical_devices/1240EHT_final.pdf>.

[23] WIPO, 'Patent Related Flexibilities in the Multilateral Legal Framework and Their Legislative Implementation at the National and Regional Levels' (18 August 2010) CDIP/5/4 Rev.

the patent right; and flexibilities related to the use and enforcement of the patent right. This report highlights the importance of information on patent status for countries to make policy and legislative decisions on the utilisation of these flexibilities at the national level.

This working paper conducts a detailed examination and analysis of 74 patent families involved in ten COVID-19 vaccines based on the data made available as of 9 June 2021 on VaxPaL, a COVID-19 vaccines patent database developed by the Medicines Patent Pool (MPP). It aims to derive insightful technical and legal information from this complex patent data and then present the information in a clear and accessible form.

The paper first describes the VaxPaL data with a focus on its vaccine selection and patent search and selection methodology. It then introduces the ten COVID-19 vaccines covered by the VaxPaL data, the four types of technology platforms used in their development, as well as their current global production status. Through an analytical review of the VaxPaL data, it then describes patterns and trends of innovation and patenting activities related to the ten COVID-19 vaccines, including what has been patented, who has applied for these patents, when and where these patents have been filed, and the legal status of these patent applications in various jurisdictions.

This information may provide useful background for policymakers on the significance and potential impact of these patent families with relevance for access to and production of these vaccines in their individual countries. This, in turn, may help support practical assessments as to potential options within and beyond the current TRIPS framework to promote equitable access to COVID-19 vaccines.

3 MPP VAXPAL – DATA COLLECTION AND SEARCH METHODLOGY[24]

On 9 June 2021, the MPP launched VaxPaL, a patent database on COVID-19 vaccines. VaxPaL contains patent information of 74 patent families filed by 20 entities from 1996 to 2021 in 105 jurisdictions. These 74 patent families claim inventions related to ten COVID-19 vaccines per se,[25] rather than technologies related to vaccine production and distribution process, such as software[26] and cold chain technologies.[27]

This section introduces VaxPaL vaccine selection, patent data search and selection methodology, which is essential for understanding the scope and limitation of VaxPaL.[28] In particular, the 74 patent families provided in VaxPaL by no means should be considered exhaustive or complete, since COVID-19 vaccines-related innovation and patenting activities are highly dynamic and fluid. VaxPaL is updated on a regular basis according to the publication or change in legal status of patent applications and development of new COVID-19 vaccines.

[24] This section is based on the information available on MPP website, and interviews with Ms Amina Maillard, Patent Information Manager, the Medicines Patent Pool in Geneva, Switzerland from July to December 2021.

[25] MPP, 'VaxPaL – COVID-19 Vaccines Patent Landscape' (9 June 2021) <https://medicinespatentpool.org/uploads/2021/06/VaxPaL_COVID-19_Vaccines-Patent-Landscape_09.06.2021.xlsx>.

[26] Chris Newmarker, 'These technologies are speeding COVID-19 vaccines to market' (Pharmaceutical Processing World, 8 April 2021) <www.pharmaceuticalprocessingworld.com/these-technologies-are-speeding-covid-19-vaccines-to-market/> accessed 24 November 2021.

[27] UN Environment Programme and IIR, 'Cold Chain Technology Brief: Vaccines' <https://wedocs.unep.org/bitstream/handle/20.500.11822/36732/CCV_EN.pdf?sequence=4&isAllowed=y> accessed 26 October 2021.

[28] MPP, 'VaxPaL' <https://medicinespatentpool.org/what-we-do/vaxpal/> accessed 10 October 2021. The scope and limitation of VaxPaL is explained in MPP Disclaimer: "Users should NOT consider VaxPaL (VaxPaL–COVID-19 vaccines patent landscape) a complete and authoritative source of patent information, and it is not meant to provide a freedom-to-operate' analysis. It only provides a snapshot at a point in time, based on the information available to MPP. We do not accept any legal responsibility for the accuracy of data. In particular, we do not guarantee it is complete, up to date or fit for specific purposes. Users should undertake additional country search and legal analysis before making any decision based on this data. A full understanding of the patent situation in any country, for a specific vaccine, requires additional information and analysis not provided in this database. This includes an analysis of the specific claims of a national/regional patent application or granted patent."

This paper is based the analysis of the VaxPaL data released on 9 June 2021.[29] While this analysis makes extensive use of the VaxPaL data, as a carefully selected data set, it should not be considered as independently endorsing or validating the accuracy and completeness of these data.

3.1 Vaccine selection

VaxPaL contains the patent information of ten COVID-19 vaccines (see Table 1), selected in line with the WHO Emergency Use Listing (EUL) and/or Prequalification (PQ) processes.

On 1 October 2020, the WHO launched an invitation to COVID-19 vaccine manufacturers to submit an Expression of Interest (EOI) for the EUL and/or PQ processes.[30] The WHO EUL procedure aims to expedite the assessment of new and unlicensed vaccines, therapeutics, and diagnostics for use during public health emergencies, based on limited data.[31] The EUL is a key tool for companies to submit their products for approval for emergency use which are not yet ready for the full WHO PQ process. Following EUL - which only provides a time-limited listing in an emergency context - the PQ process then evaluates additional clinical data on a rolling basis to ensure that the medical products meet the quality standards for broader availability.[32]

On 23 April 2021, 19 vaccines were accepted for the WHO EOI process, but only ten vaccines' dossiers were confirmed for further review:[33] BNT162b2 (Pfizer/BioNTech), AZD1222 (AstraZeneca/Oxford), Ad26.COV2-S (J&J), mRNA-1273 (Moderna), BBIBP-CorV (Sinopharm/Beijing), Coronavac (Sinovac), Covaxin (Bharat/ICMR), NVX-CoV2373 (Novavax), Sputnik V (Gamaleya), and CVnCoV (CureVac). By December 2021, the first eight vaccines had been approved for the WHO EUL, while the review of Sputnik V (Gamaleya) was still ongoing. CVnCoV (CureVac) had been withdrawn by its originator.[34]

Table 1: Ten COVID-19 vaccines selected in VaxPaL

Vaccine Technology	Vaccine Name	Originator Company[35]
Whole virus (inactivated)	Covaxin	Bharat Biotech and Indian Council of Medical Research (Bharat/ICMR)
	BBIBP-CorV	Sinopharm and Beijing Institute of Biological Products (Sinopharm/Beijing)
	Coronavac	Sinovac
Viral vector(s)	AZD1222	AstraZeneca and the University of Oxford
	Sputnik V	Gamaleya Research Institute
	Ad26.COV2-S	Janssen Pharmaceuticals (J&J)
Protein subunit	NVX-CoV2373	Novavax
Nucleic acid (mRNA)	CVnCoV	CureVac
	mRNA-1273	Moderna
	BNT162b2	Pfizer and BioNTech

[29] Since 9 June 2021, VaxPaL has only been updated once in December 2021. The updates consisted of the addition of one patent family relating to mRNA-1273 (Moderna) and patent information on three new vaccines, i.e. Ad5-nCoV (CanSino), CoV2 preS dTM-AS03 (GSK/Sanofi), and SCB-2019 (Clover). The three new vaccines have been accepted for the WHO EOI process, but none have been approved for the WHO EUL as of December 2021. Thus, the updates did not change the patterns and trends of innovation and patenting activities of the ten COVID-19 vaccines considerably, and hence, the analysis and key findings presented in this paper remain relevant. WHO (n 3).

[30] WHO, 'First Invitation to manufacturers of vaccines against Covid-19 to submit an Expression of Interest (EOI) for evaluation by the WHO (Prequalification and/or EUL)' (1 October 2020) <www.who.int/news-room/articles-detail/1-EOI-Covid-19-Vaccines> accessed 13 October 2021.

[31] WHO, 'Emergency use listing' <www.who.int/teams/regulation-prequalification/eul> accessed 12 October 2021.

[32] WHO, 'Welcome to Vaccines Prequalification' <https://extranet.who.int/pqweb/vaccines> accessed 12 October 2021.

[33] WHO (n 3).

[34] ibid. In October 2021, CureVac withdrew CVnCoV, its first-generation mRNA COVID-19 vaccine candidate, from regulatory review, and decided to focus on the second-generation mRNA vaccine in collaboration with GSK. See CureVac, 'CureVac to Shift Focus of COVID-19 Vaccine Development to Second-Generation mRNA Technology' (12 October 2021) <www.curevac.com/en/2021/10/12/curevac-to-shift-focus-of-covid-19-vaccine-development-to-second-generation-mrna-technology/>.

[35] As defined in VaxPaL, "originator company" means the company that has developed and/or is marketing the vaccine concerned.

3.2 Patent data collection and search methodology[36]

The VaxPaL data was selected through four steps: (1) collecting basic information; (2) product study, i.e. analysis of vaccine products to identify keywords and remove off-topic subject matter; (3) patent search, i.e. searching for patent applications and granted patents in publicly available databases; and (4) selecting relevant patents and inspecting their legal status in different jurisdictions.

Step 1: Collecting basic information

The first step was to collect basic information on these ten vaccines and their originator companies. This information includes: (1) regulatory approval information, product labels, vaccine constructs and their preparations, compositions, ingredients used in the compositions, and therapeutic indications; (2) technology involved in the preparation of vaccines; (3) innovators, other companies, or third parties involved in the development and manufacturing of vaccines to help identify potential patent applicants different from the originator companies[37]; and (4) patent information disclosed by the originator companies.

The information was mainly collected from the originator companies' websites, such as their annual reports and press releases, public databases, such as the US Food and Drug Administration, European Medicines Agency, WHO, national regulatory agencies, clinical trials databases, and scientific literature.

Step 2: Product study

The next step was to conduct an in-depth analysis of the vaccine information collected at the first step. It includes the analysis of the composition of the vaccine, the role of excipients used in the vaccine, the underlying technology and its applicability, and - if applicable - key modifications made in the vaccine to enhance pharmacological effect and to facilitate the method of preparation. This step is important to delimit patent search and to extract keywords for the next steps.

Step 3: Patent search

The third step in the development of the data set was patent search by using the keywords identified in the first and second steps, including originator company's name, inventor's name, vaccine candidate, excipient combination, technical names, and vaccine patent classification codes. The scope of search included publicly available patent databases, such as WIPO PATENTSCOPE, European Patent Office (EPO) Espacenet, United States Patent and Trademark Office (USPTO) Full-Text and Image Database (PatFT), the Google Patents database, and originator companies' annual reports.

Step 4: Selecting relevant patents and inspecting their legal status in different jurisdictions

The final step was to select relevant patents, map them to vaccine candidates, and collect information on the legal status of corresponding patent family members (equivalent patents and patent applications) in countries around the world. The legal status information was collected from publicly available patent databases, including national and regional patent registers.

3.3 Information in VaxPaL

The VaxPaL data at the time of consultation was contained in an Excel workbook. A main worksheet titled "Patent Families" regrouped all patent families identified as being relevant or potentially relevant to the ten COVID-19 vaccines.[38] This worksheet provided information on vaccine type, vaccine name, originator company, patent family publication number, expected expiry date (generally 20 years after the first filing date), patent applicant/assignee, legal status, and subject

[36] This section is based on the information provided by the MPP. The searching and analysis of patent data was commissioned to iProPAT Intellectual Property Solutions by the MPP. Interview with Amina Maillard (n 24).

[37] A patent applicant is an entity or individual that files a patent application, which can be either an inventor or his assignee.

[38] A patent family is a collection of national patents and patent applications covering the same or similar technical content or invention.

matter. Alongside the main worksheet, ten subsidiary worksheets presented the legal status of patent families relating to each of the ten individual vaccines in different jurisdictions.[39]

4 OVERVIEW OF TEN COVID-19 VACCINES: TECHNOLOGY PLATFORMS AND CURRENT MANUFACTURING

Four technology platforms have been deployed for COVID-19 vaccine development: whole virus (inactivated and attenuated), protein subunit, viral vector, and nucleic acid (DNA, RNA, and mRNA). These four technology platforms use different methods to trigger human's own immune system to recognize and respond to COVID-19. Each method has its own advantages and disadvantages in terms of technology maturity, vaccine efficacy, manufacturing complexity, production cost and product stability (see Table 2).

4.1 Overview of four technology platforms for COVID-19 vaccine development

Whole virus (inactivated and attenuated)

Among the four technology platforms, whole virus vaccine is the most conventional and thus the most mature technology. Based on the discovery that a similar but weaker cowpox virus extracted from animals can trigger the human immune response to the more deadly smallpox virus, Edward Jenner developed the first vaccine against smallpox at the end of the 18th century.[40] This idea led to the development of the first weakened (attenuated) vaccine against rabies in 1885, and the first destroyed (inactivated) vaccine against typhoid in 1896.[41] In general, inactivated virus vaccines are safer than attenuated ones, but they provide a weaker immune response, and thus typically require booster shots.[42]

As the most conventional type of vaccine, one distinct advantage presented by whole virus vaccine is the relative ease of manufacture at a large scale given that the supply of raw materials is normally sufficient, and the production methods are well known.[43] This advantage has been evidenced by the large-scale production of two whole virus-based COVID-19 vaccines: BBIBP-CorV (Sinopharm/Beijing) and Coronavac (Sinovac) (see section 4.2). As another advantage, whole virus vaccine, in particular inactivated vaccine, is relatively stable. For example, Coronavac (Sinovac) can be stored at normal fridge temperatures of 2-8°C and may remain stable for up to three years.[44] Thus, whole virus vaccine is a preferable option for regions with limited access to refrigeration.

However, since different viruses require different manufacturing processes, the manufacturing of whole virus vaccines requires specialized laboratory facilities (e.g. fertilized eggs, cells, or bioreactors) to cultivate, isolate, purify, and attenuate or inactivate viruses safely, which unavoidably increase costs and production time.[45]

Protein subunit

Protein subunit is also a well-established vaccine technology. Instead of using a whole virus, this type of technology only uses specific parts or fragments (subunits) of the virus that the immune system needs to recognize and induce an immune response. The utilization of parts of the virus

[39] It should be noted that, among the 74 patent families, the relevance of 12 patent families to the COVID-19 vaccines needs to be assessed based on further technical information and their legal status is therefore not provided in VaxPaL. Interview with Amina Maillard (n 24).

[40] Stanley Plotkin, 'History of vaccination' (2014) 111(34) PNAS 12283 <www.pnas.org/content/pnas/111/34/12283.full.pdf> accessed 8 October 2021.

[41] ibid.

[42] Gavi, 'What are whole virus vaccines and how could they be used against COVID-19?' <www.gavi.org/vaccineswork/what-are-whole-virus-vaccines-and-how-could-they-be-used-against-covid-19> accessed 8 October 2021.

[43] Josephine Ma, 'After the coronavirus research race, vaccine producers face new hurdles' *South China Morning Post* (16 December 2020) <https://sg.news.yahoo.com/coronavirus-research-race-vaccine-producers-050721674.html> accessed 11 October 2021.

[44] Miyoung Kim, Roxanne Liu, 'Sinovac's COVID-19 vaccine induces quick immune response' *Reuters* (18 November 2020) <www.reuters.com/article/uk-health-coronavirus-sinovac-idUKKBN27X35I> accessed 8 October 2021

[45] Gavi (n 42).

rather than the whole virus makes protein subunit vaccine very safe and stable.[46] However, given the absence of pathogen-associated molecular patterns, protein subunit vaccine often triggers a weaker immune response and thus may require the addition of adjuvants and multiple doses to boost the immune response.[47]

In terms of the manufacturing process, protein subunit vaccines are relatively low cost and easy to scale up in large tanks, as they are typically made by growing antigens in yeast cells.[48] On the other hand, one of its disadvantages is that the R&D process of protein subunit vaccines usually requires a longer development timeline to identify which antigen and which adjuvant combinations are likely to be effective and to develop tailored manufacturing process for specific subunits.[49] NVX-CoV2373 (Novavax), as a typical protein subunit vaccine, was the first protein subunit-based COVID-19 vaccine submitted for WHO EUL/PQ evaluation.[50]

Viral vector

Viral vector is another well-established technology platform which scientists began researching in the 1970s.[51] Differing from the conventional whole virus or protein subunit vaccines, viral vector vaccines do not contain antigens, but rather use a modified version of a virus (a so-called 'vector', which is not the virus the vaccine aims to fight against) to deliver instructions to human cells' machinery to make antigens.[52] Many viral vector-based COVID-19 vaccines, including AZD1222 (AstraZeneca/Oxford), Ad26.COV2-S (J&J), and Sputnik V (Gamaleya) use adenovirus as their delivery system.

Since this process imitates the infection process of an actual virus, it has the advantage of triggering a relatively strong immune response without causing infection.[53] For example, Ad26.COV2-S (J&J) vaccine requires only one shot to be effective, which is a favourable option for regions with limited capacity for administering second shots. Furthermore, viral vector vaccines are relatively stable, and can typically be stored at 2-8°C.[54] However, the manufacturing process of viral vector vaccines is relatively complex, costly, and difficult to scale up as conventional viral vectors are grown on cell substrates and the process to assemble viral vectors with genetic code for antigens is complicated.[55]

Nucleic acid (DNA, RNA, and mRNA)

Nucleic acid (DNA, RNA, and mRNA) technology platform is a cutting-edge technology in comparison with the above-mentioned three technology platforms. Like viral vector vaccines, nucleic acid vaccines deliver genetic instructions into human cells to make a specific viral protein that the immune system can recognize and respond to.[56] Due to the transient nature of mRNA which can be quickly degraded, there is no risk of random genome integration, but mRNA-based vaccines may require booster shots to create long-term immunological memory.[57]

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[46] Gavi, 'What are protein subunit vaccines and how could they be used against COVID-19?' <www.gavi.org/vaccineswork/what-are-protein-subunit-vaccines-and-how-could-they-be-used-against-covid-19> accessed 8 October 2021.

[47] ibid.

[48] ibid.

[49] Cynthia A. Challener, 'Subunit Vaccines and the Fight Against COVID-19' (*BioPharm International*, 2 August 2021) <www.biopharminternational.com/view/subunit-vaccines-and-the-fight-against-covid-19> accessed 11 October 2021.

[50] WHO (n 3).

[51] Centers for Disease Control and Prevention (CDC), 'Understanding Viral Vector COVID-19 Vaccines' <www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/viralvector.html> accessed 8 October 2021.

[52] Gavi, 'What are viral vector-based vaccines and how could they be used against COVID-19?' <www.gavi.org/vaccineswork/what-are-viral-vector-based-vaccines-and-how-could-they-be-used-against-covid-19> accessed 8 October 2021.

[53] ibid.

[54] Daan J.A. Crommelin and others, 'The Science is There: Key Considerations for Stabilizing Viral Vector-Based Covid-19 Vaccines' (2021) 110(2) J Pharm Sciences 627 <https://pubmed.ncbi.nlm.nih.gov/33242452/> accessed 11 October 2021.

[55] Gavi (n 52).

[56] Gavi, 'What are nucleic acid vaccines and how could they be used against COVID-19?' <www.gavi.org/vaccineswork/what-are-nucleic-acid-vaccines-and-how-could-they-be-used-against-covid-19> accessed 8 October 2021.

[57] ibid.

Compared with the other vaccine technologies, one significant advantage of nucleic acid technology, in particular mRNA, is its precision, as it only expresses a specific antigen and triggers a direct immune response. Another advantage is the flexibility in enabling an established platform to be swiftly redeployed to design and test new vaccines based on new viral sequences, which is instrumental in speeding up vaccine development.[58] In fact, two mRNA-based COVID-19 vaccines, BNT162b2 (Pfizer/BioNTech) and mRNA-1273 (Moderna), were the first vaccines approved by the WHO EUL for emergency use during the COVID-19 pandemic.[59] In addition, it is relatively easy and cost effective to manufacture DNA and mRNA-based vaccines because both DNA and mRNA can be synthesized chemically and the same facilities can be used to manufacture different vaccines.[60]

However, as one disadvantage, some mRNA vaccines require extremely cold temperatures for their storage. For example, BNT162b2 (Pfizer/BioNTech) needs to be shipped at temperatures between -90 to -60°C.[61] mRNA-1273 (Moderna) needs to be stored between -50 to -15°C.[62] When stored between 2-8°C, these vaccines will expire within one month.[63]

Table 2: Comparisons between four technology platforms for COVID-19 vaccines development

	Whole virus		Protein subunit	Viral vector	Nucleic acid (DNA, RNA, and mRNA)
	Inactivated	Attenuated			
Technology maturity	Well-established	Well-established	Well-established	Well-established	Relatively new
Efficacy (immune response)	Adjuvants and booster shots may be required	Strong immune response	Adjuvants and booster shots may be required	Strong immune response (but previous exposure to vector could reduce efficacy)	Booster shots may be required
Difficulty to manufacture	Relatively simple	Relatively simple	Relatively simple	Relatively complex	Relatively simple
Cost to manufacture	Relatively costly (specialized equipment)	Relatively costly (specialized equipment)	Relatively low-cost	Relatively costly (assembling process)	Relatively low-cost
Storage conditions (stability)	Relatively stable	Relatively temperature sensitive	Relatively stable	Relatively stable	Some mRNA vaccines require ultra-cold storage
COVID-19 vaccines	• Covaxin (Bharat/ICMR) • BBIBP-CorV (Sinopharm/ Beijing) • Coronavac (Sinovac)		• NVX-CoV2373 (Novavax)	• AZD1222 (AstraZeneca/Oxford) • Sputnik V (Gamaleya) • Ad26.COV2-S (J&J)	• CVnCoV (CureVac) • BNT162b2 (Pfizer/BioNTech) • mRNA-1273 (Moderna)

Source: Authors' compilations based on Gavi, 'There are Four Types of COVID-19 Vaccines: Here's How They Work' <www.gavi.org/vaccineswork/there-are-four-types-covid-19-vaccines-heres-how-they-work> accessed 8 October 2021.

[58] Sara Sousa Rosa and others, 'mRNA Vaccines Manufacturing: Challenges and Bottlenecks' (2021) 39(16) Vaccine 2190 <https://pubmed.ncbi.nlm.nih.gov/33771389/> accessed 8 October 2021.

[59] ibid.

[60] Gavi (n 56).

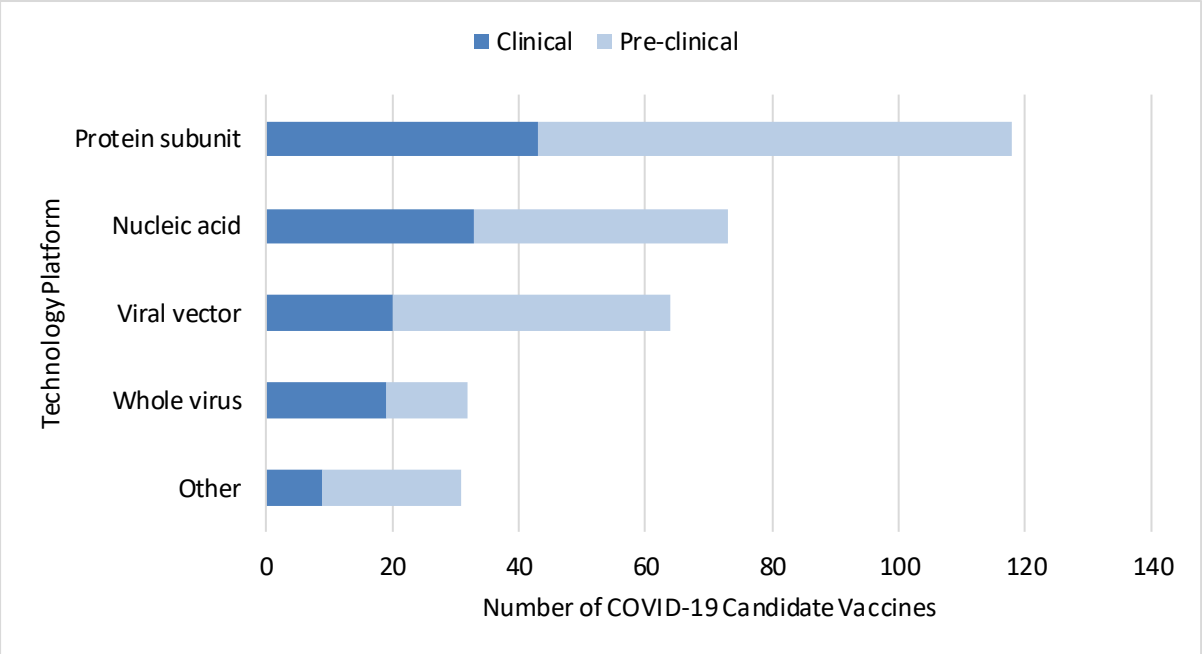
[61] CDC, 'Pfizer-BioNTech COVID-19 Vaccine Storage and Handling Summary' <www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/downloads/storage-summary.pdf> accessed 11 October 2021.

[62] CDC, 'Moderna COVID-19 Vaccine: Storage and Handling Summary' <www.cdc.gov/vaccines/covid-19/info-by-product/moderna/downloads/storage-summary.pdf> accessed 11 October 2021.

[63] CDC (n 61); CDC (n 62).

According to WHO's COVID-19 Vaccine Tracker and Landscape, as of 5 October 2021, protein subunit is the most widely used technology platform, with 43 vaccine candidates in clinical phase and 75 in pre-clinical phase (see Figure 1).[64] The second one is nucleic acid which has a total of 33 candidates in clinical trials phase and 40 in preclinical phase. In addition, there are 20 viral vector-based vaccine candidates in clinical phase and 44 under pre-clinical development. Whole virus technology was deployed in the development of 19 candidates in clinical phase (17 inactivated and two attenuated vaccines) and 13 pre-clinical candidates. These constitute a total of 124 COVID-19 vaccine candidates in clinical development and 194 in pre-clinical development.

Figure 1: COVID-19 vaccine candidates in development



Source: WHO, 'COVID-19 Vaccine Tracker and Landscape', <www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines> accessed 5 October 2021.

4.2 Current manufacturing of COVID-19 vaccines based on four technology platforms

As shown in Figure 2, the ten COVID-19 vaccines selected in VaxPaL have contributed to over 10.8 billion doses as of 31 December 2021, which account for more than 99% of the global COVID-19 vaccine production. Among these 10.8 billion doses, more than 2.4 billion doses are Coronavac (Sinovac), followed by AZD1222 (AstraZeneca/Oxford), BNT162b2 (Pfizer/BioNTech), and BBIBP-CorV (Sinopharm/Beijing) with each having produced approximately 2 billion doses. There are also more than 600 million doses of mRNA-1273 (Moderna), 289 million doses of Ad26.COV2-S (J&J), 273 million doses of Sputnik V (Gamaleya), 201 million doses of Covaxin (Bharat/ICMR), and nine million doses of NVX-CoV2373 (Novavax).

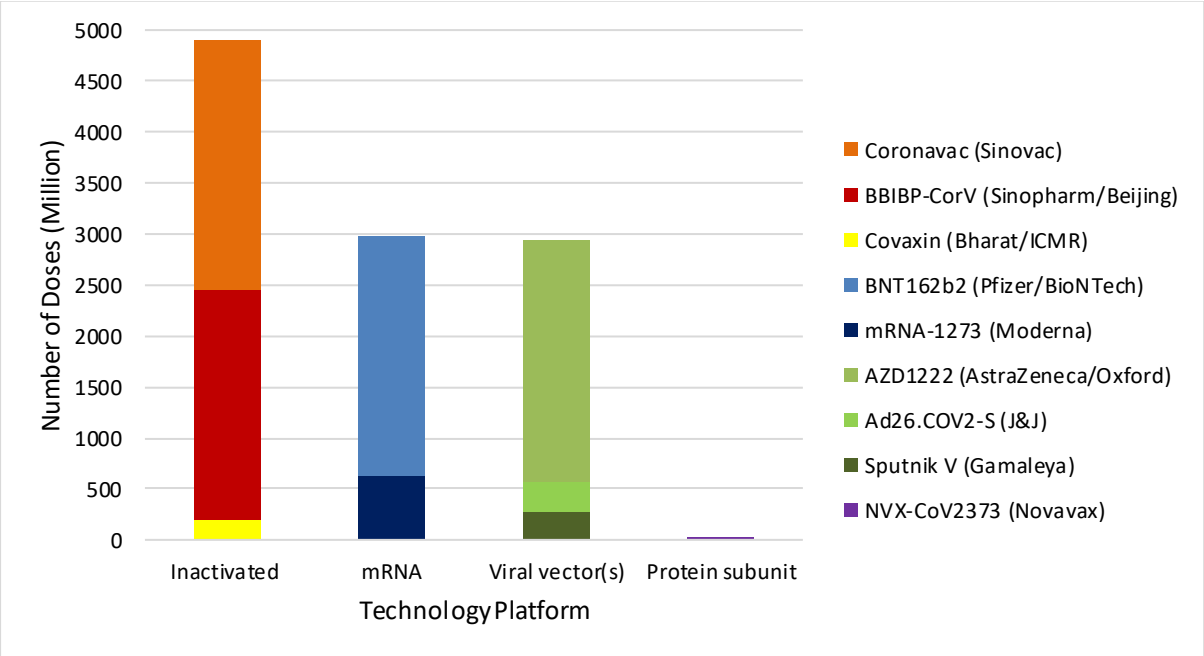
There is no production data on CVnCoV (CureVac). As mentioned before, CureVac withdrew CVnCoV from regulatory review in October 2021. Novavax announced a promising phase 3 trial result in January 2021: although clinical trials showed that NVX-CoV2373 (Novavax) has similar efficacy against the virus as mRNA-based vaccines, quality control issues at Novavax's manufacturing sites have delayed its regulatory approval process.[65] Only a few protein subunit-based vaccines have been submitted to the WHO EUL/PQ evaluation process and NVX-CoV2373 (Novavax) has been

[64] WHO, 'COVID-19 Vaccine Tracker and Landscape' <www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines> accessed 5 October 2021.

[65] Grady McGregor, 'Novavax vaccine could outperform mRNAs—if it can solve manufacturing delays' (*Fortune*, 24 September 2021) <https://fortune.com/2021/09/24/novavax-who-approval-covid-vaccine-mrna-covax/>.

approved for the WHO EUL in December 2021, while protein subunit technology has been used to develop almost 40% of COVID-19 vaccine candidates (see Figure 1).

Figure 2: Ten selected COVID-19 vaccine production



Source: Authors' compilations based on Airfinity, 'COVID-19' <www.airfinity.com/areas/covid-19> accessed 12 January 2022.
Note: No production data for CVnCoV (CureVac).

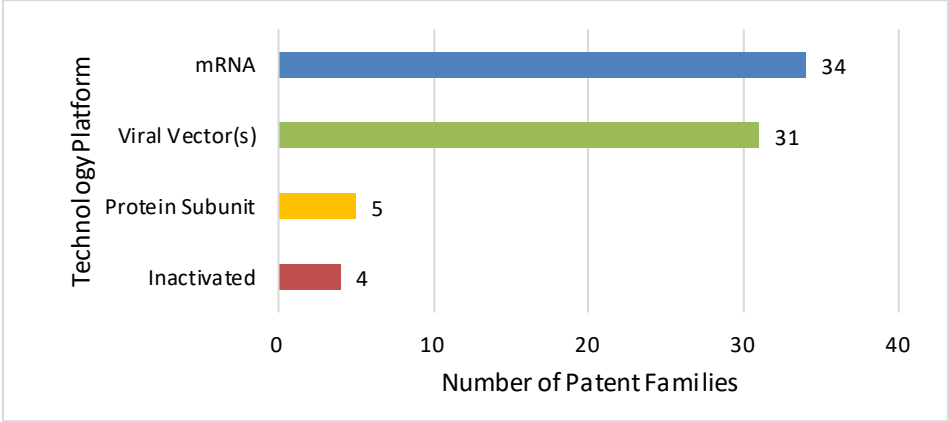
5 INNOVATION AND PATENTING ACTIVITIES OF COVID-19 VACCINES

According to the VaxPaL data, during the period from 1996 to 2021, 74 patent families have been filed by 20 entities in 105 jurisdictions. This section conducts a statistical analysis of these 74 patent families with a breakdown by type of technology platform, nature of patent applicant, year of first application, office of first filing, and office of subsequent filing. It also provides an overview of the legal status of the 74 patent families in the various jurisdictions.

5.1 Innovation and patenting activity by vaccine technology platform

As described in section 4, four technology platforms have been deployed for the development of the ten COVID-19 vaccines: whole virus (inactivated and attenuated), protein subunit, viral vector, and nucleic acid (DNA, RNA, and mRNA). Among these four technology platforms, mRNA is the most patent-intensive one in terms of the number of patent families concerned, with a total of 34 patent families filed for three mRNA-based vaccines (see Figure 3). Viral vector is slightly less patent-intensive than mRNA, aggregately involving 31 patent families. At the other end, protein subunit and inactivated are the least patent intensive, involving only five and four patent families respectively.

Figure 3: Number of patent families by type of vaccine technology platform



Source: Authors' calculations based on VaxPaL data.

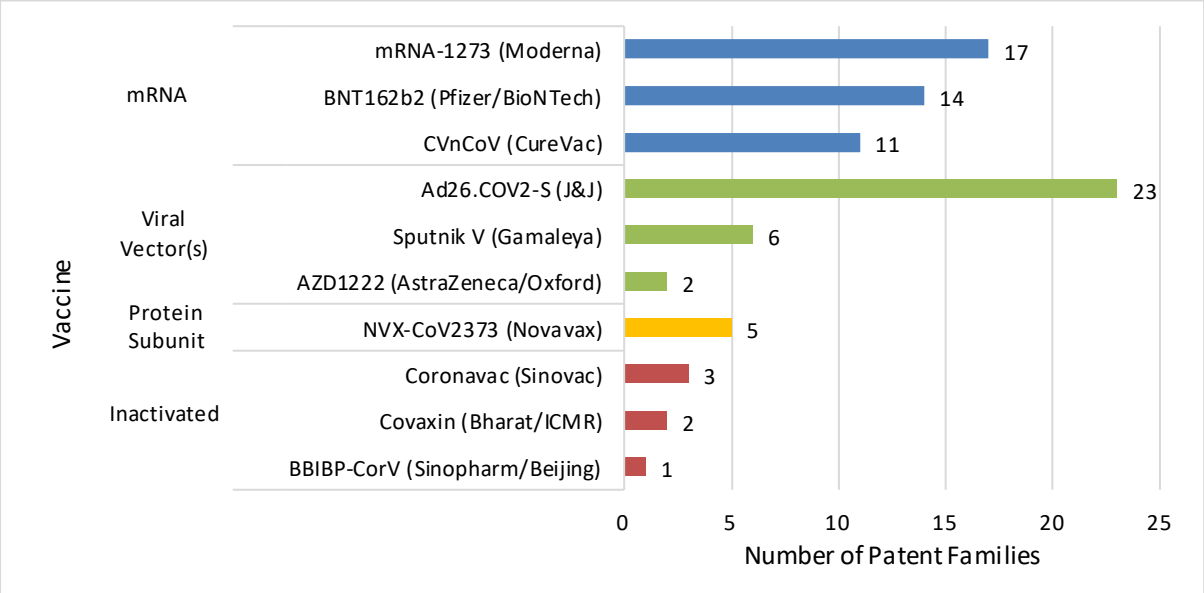
Ad26.COV2-S (J&J), a viral vector-based vaccine, is the most patent-intensive of the vaccine technologies, covered by 23 patent families. It is followed with decreasing patent intensiveness by the three mRNA-based vaccines: mRNA-1273 (Moderna) with 17 patent families, BNT162b2 (Pfizer/BioNTech) with 14 patent families, and CVnCoV (CureVac) with 11 patent families (see Figure 4).

The other two viral vector-based vaccines, Sputnik V (Gamaleya) and AZD1222 (AstraZeneca/Oxford), are much less patent-intensive than Ad26.COV2-S (J&J). They are only covered by six and two patent families respectively, which indicates a wide variation of patent intensity even between the vaccines based on the same technology platform.

NVX-CoV2372 (Novavax), as the only one protein subunit-based vaccine in VaxPaL, is covered by five patent families.

Unsurprisingly, the three inactivated vaccines, Coronavac (Sinovac), Covaxin (Bharat/ICMR), and BBIBP-CorV (Sinopharm/Beijing), are the least patent-intensive vaccines compared with those based on the three other platforms. Each of them is covered by three or less patent families, according to these data.

Figure 4: Number of patent families by each COVID-19 vaccine



Source: Authors' calculations based on VaxPaL data.

The aggregate number of patent families shown in Figure 4 is 84, which is higher than the 74 patent families identified in VaxPaL. The difference of ten is owing to the fact that eight patent families have been covered in more than one vaccine.

As shown in Table 3, among these eight patent families, seven are mRNA related, which exhibits a complex patent landscape behind mRNA-based COVID-19 vaccines.[66] These shared patent families typically reveal basic scientific discoveries or represent fundamental scientific advancements, and thus have the potential to be widely used in developing new vaccines or other medical products in the future.

For instance, both mRNA-1273 (Moderna) and BNT162b2 (Pfizer/BioNTech) are covered by two patent families that were filed by the Trustees of the University of Pennsylvania. These patent families disclosed that the modified mRNA can avoid immediate immune detection and enter into target cells, paving the way for mRNA-based vaccines.[67] In addition, patent families filed by Protiva and Acuitas, which mainly include key lipid nano-particle technologies serving as a delivery system for mRNA, were widely used in more than one mRNA vaccine.

It should be noted that Table 3 does not necessarily imply any licensing or technology transfer arrangement between the patent applicants and the vaccine originators. In fact, some of them are involved in patent validity disputes, which indicates the dynamic nature of legal status of these patent families. For instance, Moderna has initiated three *inter partes* review proceedings at the Patent Trial and Appeal Board (PTAB) against Arbutus's US patents (which were originally filed by Protiva and later assigned to its successor Arbutus), including US Patents No. 9,364,435 and 8,058,069 (corresponding to WIPO's WO 2009/127060 family) and US Patent No. 9,404,127 (corresponding to WO 2012/000104 family).[68]

Table 3: Patent families involved in multiple COVID-19 vaccines

Vaccine (originator) / Patent Applicant / Patent Number		mRNA			Inactivated		
		mRNA-1273 (Moderna)	BNT162b2 (Pfizer/ BioNTech)	CVnCoV (CureVac)	BBIBP-CorV (Sinopharm/ Beijing)	Covaxin (Bharat/ ICMR)	Coronavac (Sinovac)
University of Pennsylvania	WO 2007/024708	■	■				
	WO 2014/160243	■	■				
Protiva (Arbutus)	WO 2009/127060	■	■				
	WO 2012/000104	■	■				
Acuitas	WO 2015/199952		■	■			
	WO 2017/075531 WO 2018/081480		■	■			
	WO 2021/030701	■	■	■			
Wuhan Institute of Biological Products	CN 111569058 A				■	■	■

Source: Authors' compilations based on VaxPaL data.

[66] Mario Gaviria and Burcu Kilic, 'A Network Analysis of COVID-19 mRNA Vaccine Patents' (2021) 39 Nature Biotechnology 546 <www.nature.com/articles/s41587-021-00912-9> accessed 9 October 2021.

[67] Drew Weissman and Katalin Karikó, 'University of Pennsylvania mRNA Biology Pioneers Receive COVID-19 Vaccine Enabled by their Foundational Research' (*PennMedicine News*, 23 December 2020) <www.pennmedicine.org/news/news-releases/2020/december/penn-mrna-biology-pioneers-receive-covid19-vaccine-enabled-by-their-foundational-research> accessed 9 October 2021.

[68] Dylan Haversack and Daniel Shores, 'COVID-19 Vaccine Leader Moderna "Not Aware of Any Significant Intellectual Property Impediments" in Development of its Vaccine Despite Mixed Results at PTAB' (*JDSUPRA*, 16 November 2020) <www.jdsupra.com/legalnews/covid-19-vaccine-leader-moderna-not-81369/> accessed 9 October 2021. It should be highlighted that this paper does not seek to evaluate the legal validity of any patent or the legal sufficiency of any patent infringement claims and should not be interpreted as such.

5.2 Patenting activity by nature of patent applicant

This section examines the nature of patent applicants of the 74 patent families. For this purpose, patent applicants are grouped into four categories: private enterprises, universities, public research institutions, and non-profit organizations.[69]

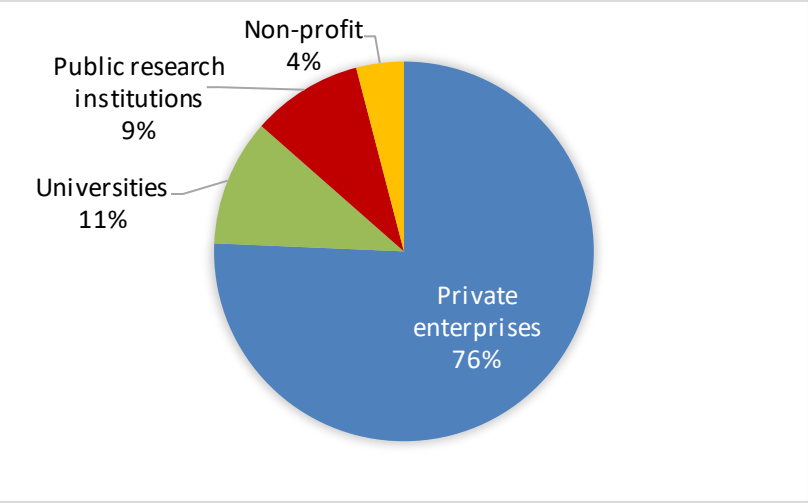
Among the 74 patent families, three have not yet been published, so their applicants are still not available in VaxPaL and thus excluded from the following examination.[70] Among these 71 patent families, 68 have a single patent applicant, and three have two joint applicants. Thus, the cumulative sum of patent applicants is 74.

Figure 5 shows that 76% of these 74 patent applicants (56) are private enterprises in the biotechnology and pharmaceutical industry. In comparison, only 11% of the patent applicants are universities and their trustees and subsidiaries, such as Oxford University Innovation Limited, a wholly owned subsidiary of the University of Oxford. 9% of the patent applicants are public research institutions, namely Gamaleya Research Institute (under the Ministry of Health of the Russian Federation) and the Wuhan Institute of Biological Products (a subsidiary of Sinopharm, a Chinese state-owned enterprise). Non-profit organizations represent 4% of all the patent applicants.

In light of the above-mentioned distribution of the 71 patent families among the four categories of patent applicants, private enterprise has evidently played a dominant role in patenting activities covering the ten COVID-19 vaccines. However, while public research institutions and universities have fewer patent applications than private enterprise players, they have played a critical role in the vaccine development through conducting basic scientific research (see Table 3).

Research collaboration across these four categories of applicants is observable in the development of vaccine technology. In total, there are three patent families jointly filed by different types of patent applicants: two jointly filed by university (Leiden University) and private enterprise (Introgene, a spinoff from Leiden University), and one jointly filed by private enterprise (BioNTech) and a non-profit organization (Translational Oncology (TRON) at the University Medical Center of the Johannes Gutenberg University Mainz).

Figure 5: Percentage of different types of patent applicants involved in 71 patent families



Source: Authors' calculations based on VaxPaL data.
Note: This figure is based on the cumulative sum of patent applicants (74) rather than the number of patent families (71).

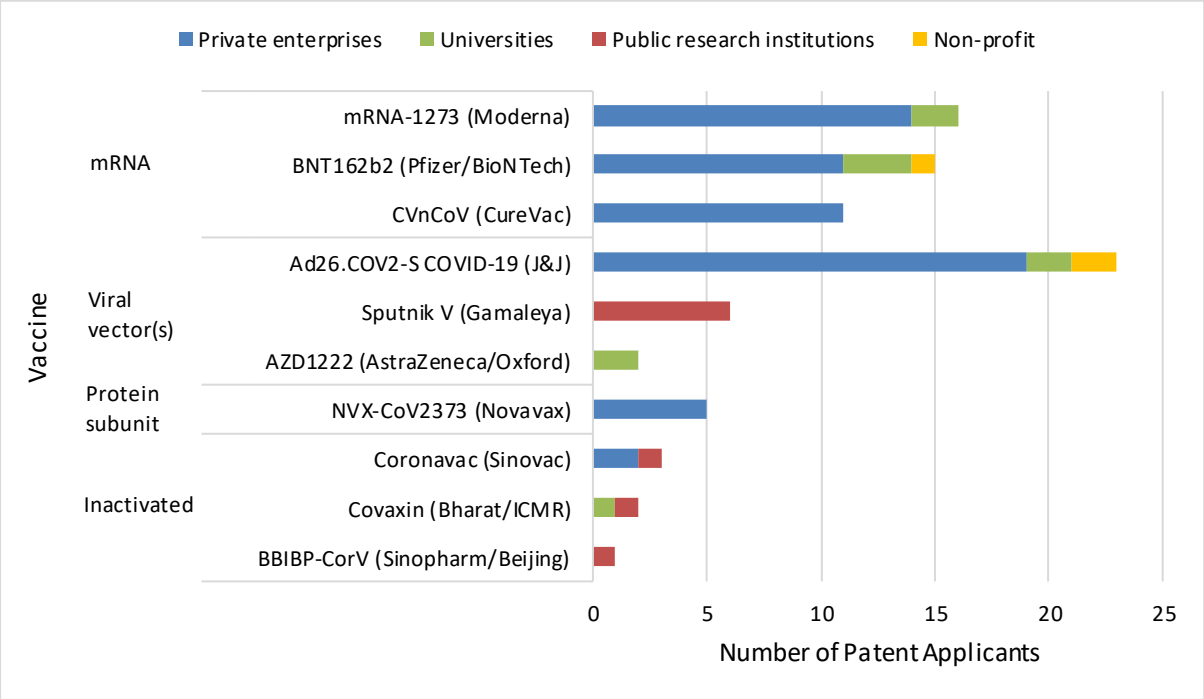
[69] See Samuel Cross and others, 'Who Funded the Research Behind the Oxford-AstraZeneca COVID-19 Vaccine?' (*MedRxiv*, 10 April 2021) <www.medrxiv.org/content/10.1101/2021.04.08.21255103v1.full.pdf> accessed 10 October 2021.

[70] Among the three unpublished patent applications, two are related to Ad26.COV2-S (J&J) and one is related to mRNA-1273 (Moderna). The information on these unpublished patent applications was mainly collected through originator companies' press releases and inventors' scientific publications. Interview with Amina Maillard (n 24).

Figure 6 demonstrates the contribution of the four types of patent applicants to the development of each of the ten COVID-19 vaccines. Six out of ten involve private enterprises, which are the three mRNA-based vaccines and one from each of the other three platforms: viral vector, protein subunit, and inactivated whole virus. These six vaccines account for approximately 53% of the global COVID-19 vaccine production (see Figure 2). Among these six vaccines, four have patents filed by universities, public research institutions, or non-profit organizations, including BNT162b2 (Pfizer/BioNTech) and Ad26.COV2-S (J&J), both of which involve three different types of patent applicants.

The other four vaccines, Sputnik V (Gamaleya), AZD1222 (AstraZeneca/Oxford), Covaxin (Bharat/ICMR), and BBIBP-CorV (Sinopharm/Beijing) only involve patents from public research institutions and universities. They cover approximately 47% of the global vaccine production (see Figure 2).

Figure 6: Type and number of patent applicants in each COVID-19 vaccine



Source: Authors' calculations based on VaxPaL data.

Figure 7 is a list of all patent applicants involved in the ten COVID-19 vaccines according to the number of patent families filed. For mRNA vaccines, Moderna is the most active applicant, having filed 11 patent families, followed by CureVac with six patent families, Acuitas with five patent families, Protiva (Arbutus's predecessor) with four patent families, the Trustees of the University of Pennsylvania with three patent families, BioNTech with three patent families (including one jointly filed with TRON), and Polymun with one patent family.

Among the 31 patent families covering viral vector technology, 21 are related to Ad26.COV2-S (J&J), not including two unpublished applications as indicated above. Of these 21 patent families, 13 patent families were filed by Crucell (a small Netherlands-based biopharmaceutical company acquired by J&J in 2011), four by Janssen Vaccines (a subsidiary of J&J renamed from Crucell), two co-filed by Leiden University and Introgene (a predecessor of Crucell and a spinoff from Leiden University), and two by Brigham and Women's Hospital (a non-profit charitable institution).[71] Gamaleya Research Institute, the only patent applicant covering Sputnik V (Gamaleya), filed six patent families. Oxford University Innovation Limited is the applicant of two patent families covering AZD1222 (AstraZeneca/Oxford).

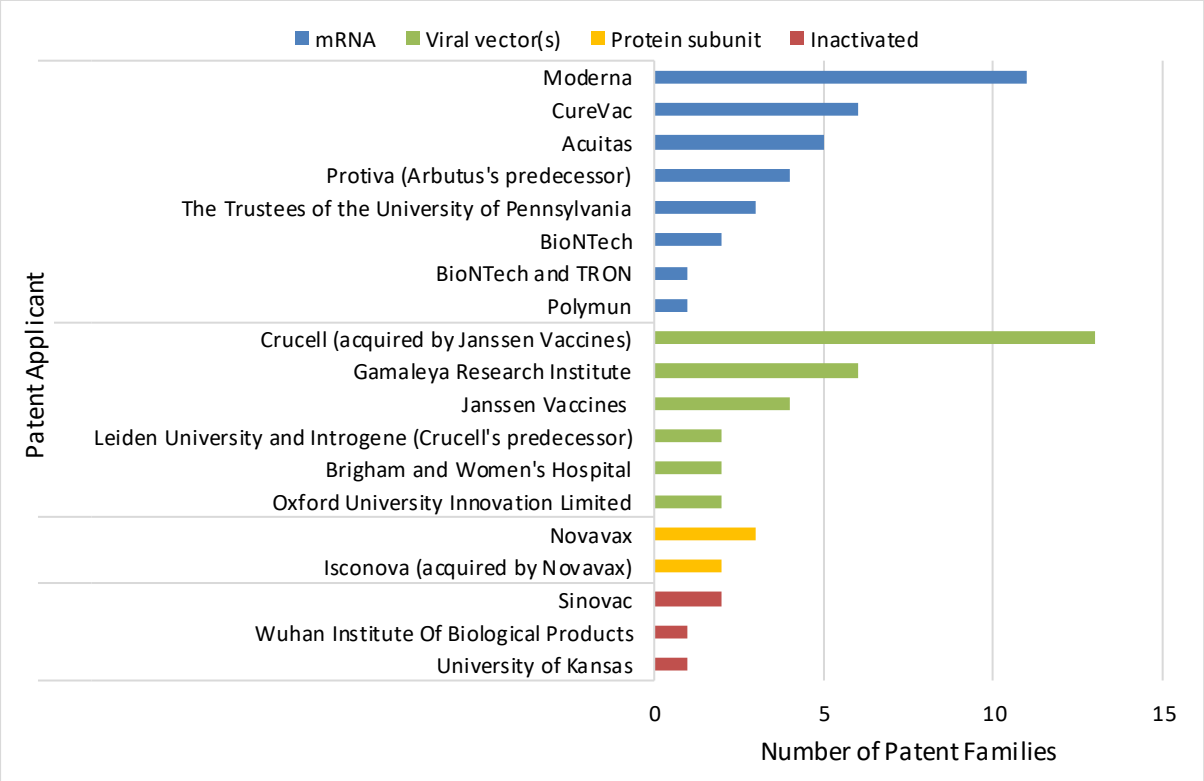
[71] BioPharm International Editors, 'AGC Biologics Acquires Cell and Gene Therapy Commercial Manufacturing Facility' (*BioPharm International*, 9 August 2021) <www.biopharminternational.com/view/agc-biologics-acquires-cell-and-gene-therapy-commercial-manufacturing-facility> accessed 9 October 2021.

The list of the top patent applicants in the four technology platforms indicates the deep involvement of private enterprises, specifically small and medium-sized enterprises (SMEs), in COVID-19 vaccine R&D.[72] These small companies usually conduct focused R&D efforts, then patent the results of these efforts, and later license or assign their patents to larger pharmaceutical companies for product development and clinical trials which usually require significant capital investment.

For example, mRNA-1273 (Moderna) is Moderna's first-ever approved product. It is based on 11 patent families filed by Moderna itself, three by other small biotech companies, Acuitas and Protiva, two by Trustees of the University of Pennsylvania, and one unpublished patent application.

Another typical example is BioNTech, a small German immunotherapy company which began developing potential mRNA COVID-19 vaccine candidates in January 2020 and then announced cooperation with Pfizer in March 2020 for clinical trials.[73] Among 14 patent families related to BNT162b2 (Pfizer/BioNTech), eight were filed by Acuitas and Protiva, three filed by BioNTech (including one jointly filed by BioNTech and TRON), and another three filed by the Trustees of the University of Pennsylvania. It is interesting to note that out of the four largest vaccine companies, only Pfizer was able to develop one COVID-19 vaccine approved for the WHO EUL, and even this was done in collaboration with BioNTech.[74] This once again proves that SMEs are at the forefront of COVID-19 vaccine R&D activities.

Figure 7: Top patent applicants in four technology platforms



Source: Authors' calculations based on VaxPaL data.

[72] According to BIO's COVID-19 Therapeutic Development Tracker, SME biotech firms (namely companies with global revenue under USD 25 million) account for roughly 75% of the pipeline of treatments and vaccines for COVID-19. BIO, 'Biotechnology Innovation Organization: 2021 Special 301 Submission' <www.keionline.org/wp-content/uploads/BIO_2021_Special_301_Review_Comment.pdf> accessed 9 October 2021.

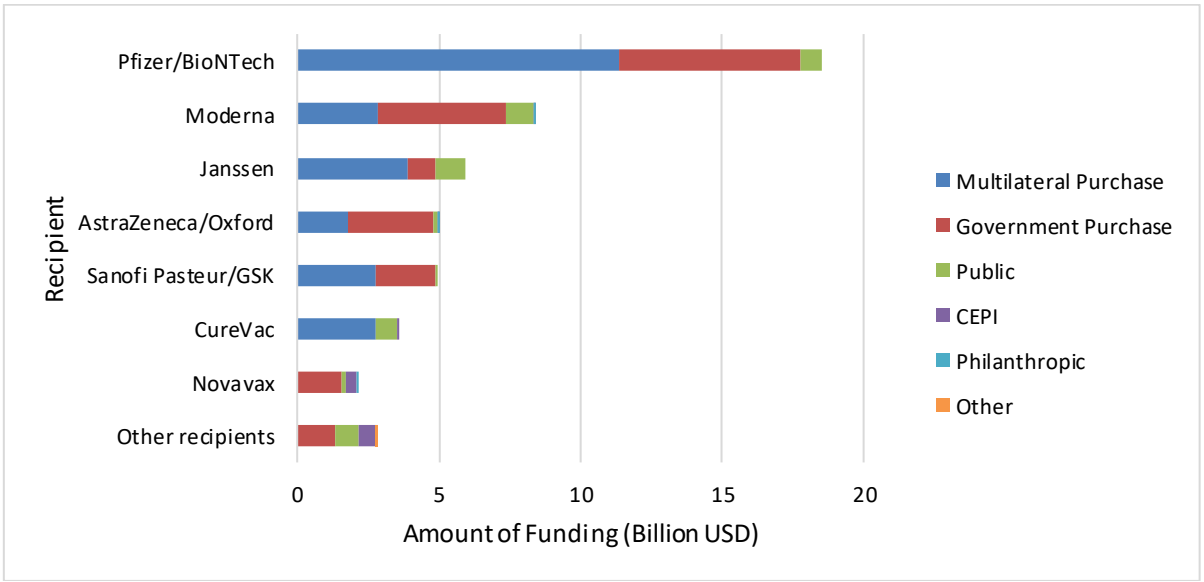
[73] Pfizer, 'Pfizer and BioNTech to Co-develop Potential COVID-19 Vaccine' (17 March 2020) <https://investors.pfizer.com/investor-news/press-release-details/2020/Pfizer-and-BioNTech-to-Co-Develop-Potential-COVID-19-Vaccine/default.aspx> accessed 10 October 2021.

[74] Before the COVID-19 pandemic, the Big Four, i.e., GSK, Sanofi, Merck, and Pfizer, dominated the vaccine market by producing 90% of revenues. Hannah Kuchler and Leila Abboud, 'Why the three biggest vaccine makers failed on Covid-19' *Financial Times* (16 February 2021) <www.ft.com/content/657b123a-78ba-4fba-b18e-23c07e313331> accessed 10 October 2021.

In addition to their own R&D investments, several private companies and universities have received significant funding from external sources, including multilateral and government advance purchase agreements (APAs)[75], other public sector support, Coalition for Epidemic Preparedness Innovations (CEPI) and philanthropic bodies, in support of their vaccine R&D and production activities, as shown in Figure 8.

Interestingly, the top patent applicants, including Pfizer/BioNTech, Moderna, Janssen (J&J), AstraZeneca/Oxford, CureVac, and Novavax, correspond, to a certain extent, with the top recipients of such external funding. Of the USD 51.1 billion investment tracked from January 2020 up to July 2021, Pfizer/BioNTech received more than 18 billion, 96% of which came from multilateral and government APAs and 4% of which was from public sector. Moderna received 8.3 billion in total with a vast majority came from APAs. Janssen also received 5.9 billion from APAs and public sector.[76]

Figure 8: Top recipients of COVID-19 vaccine R&D external funding



Source: Global Health Centre, 'COVID-19 Vaccines R&D Investments' (8 July 2021) <www.knowledgeportalia.org/covid19-r-d-funding> accessed 22 November 2021.

5.3 Patenting activity by patent first filing date

This section provides an overview of the first filing dates of the 74 patent families.[77]

The first filing date is the date when a patent application is first filed for an invention at a patent office. In many jurisdictions, the patent applicant can file his patent application within six months or one year (so-called grace period) after the first public disclosure of the invention.[78] Thus, the first filing date can be used as an indicator of the time of innovation activities surrounding a particular patent, while the actual innovation breakthrough is necessarily accomplished well before its patent first filing date.

To understand the time of COVID-19 vaccine-related innovation and patenting activities, the 74 patent families are divided into two groups according to their first filing dates: before or after

[75] APA is a purchase agreement signed between a vaccine developer and a purchasing entity before vaccine approval by a governmental regulatory agency. The funding provided through APAs might be used in R&D activities, scaling up of manufacturing capacity or acceleration of clinical development.

[76] Global Health Centre, 'COVID-19 Vaccines R&D Investments' (8 July 2021) <www.knowledgeportalia.org/covid19-r-d-funding> accessed 22 November 2021.

[77] If there are more than one patent in the same patent family and these patents are filed on different dates, the first filing date of such patent family is determined by the earliest date.

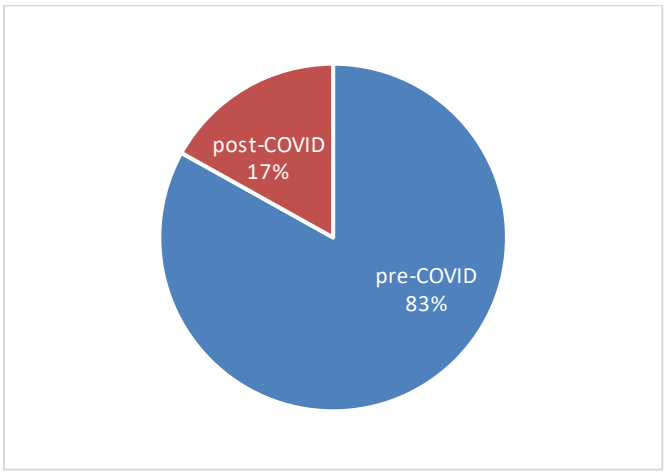
[78] WIPO, 'Certain Aspects of National/Regional Patent Laws' (October 2021) <www.wipo.int/export/sites/www/scp/en/national_laws/grace_period.pdf> accessed 9 October 2021.

31 December 2019 when the first COVID-19 case was reported.[79] These two groups of patent families are referred to as pre- and post-COVID patent hereafter.

Figure 9 demonstrates that 83% (59 out of 71) of the patent families were filed prior to 31 December 2019.[80] Only 17% were filed after this cut-off date. Among the 59 pre-COVID patents, more than half (56%) were filed between 1 January 2011 and 31 December 2019, 32% were filed between 1 January 2001 and 31 December 2010, and 12% were filed before 31 December 2000.

Given that the term of patent protection is normally 20 years from the first filing date if maintained for its full length,[81] seven patent families had already expired by the end of 2020, and two other patent families are expected to expire by the end of 2021.

Figure 9: Percentage of patent families filed before and after 31 December 2019



Source: Authors' calculations based on VaxPaL data.

As a follow-up to section 5.2 (patenting activity by nature of patent applicant), the first filing dates of the 71 patent families are further broken down according to the four categories of patent applicants, recalling that these are private enterprises, universities, public research institutions, and others (including non-profit organizations and joint applicants).[82]

Figure 10 shows that private enterprises are evidently dominant contributors in the development of pre-COVID vaccine technologies and their patent filings, while public research institutions are late movers, with seven patents filed in 2020 or 2021. Since 1996, the private sector's patent filings reached three peaks in 2004, 2013 and 2016, in each case roughly one or two years after the outbreak of each of the three major viruses: SARS, MERS, and Ebola.[83]

[79] WHO, 'Listings of WHO's response to COVID-19' <www.who.int/news/item/29-06-2020-covidtimeline> accessed 9 October 2021.

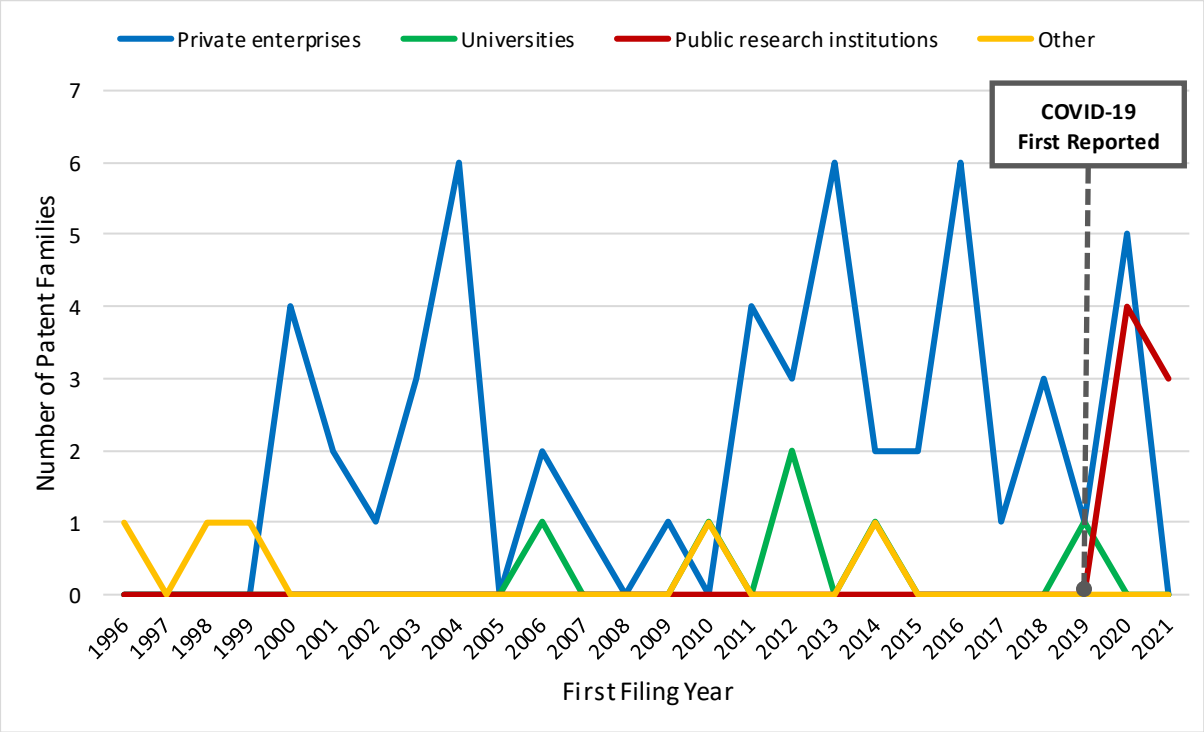
[80] There are three unpublished post-COVID patents, two of which were filed by J&J and one by Moderna. Since their filing dates are not yet available as of 9 June 2021, they are not included in this section. Nevertheless, these three patent applications will not bring any discernible change to the overall trend.

[81] According to Article 33 of the TRIPS Agreement, the term of patent protection shall not be less than 20 years counted from the filing date. Since the TRIPS Agreement entered into force in 1995, all WTO Members have the obligation to meet this minimum requirement. However, in practice, some patents are either abandoned by their owners or invalidated by administrative or judicial authorities before their expiration, while some other patents, particularly those in the pharmaceutical area, enjoy extended patent protection through legal, business, and technological strategies (so-called evergreen pharmaceutical patents).

[82] In section 5.2, patent applicants are divided into four groups: private enterprises, universities, public research institutions, and non-profit organizations in order to count the cumulative sum of patent applicants in each of these groups. This section aims to show the total number of patent families filed in each year, and thus the "other" category includes patent families that are jointly filed by different types of patent applicants.

[83] WHO, 'Severe Acute Respiratory Syndrome (SARS)' <www.who.int/health-topics/severe-acute-respiratory-syndrome#tab=tab_1>; WHO, 'Middle East respiratory syndrome coronavirus (MERS-CoV)' <www.who.int/health-topics/middle-east-respiratory-syndrome-coronavirus-mers#tab=tab_1>; WHO, 'Ebola virus disease' <www.who.int/health-topics/ebola#tab=tab_1>; WHO, 'Influenza A (H1N1)' <www.who.int/emergencies/situations/influenza-a-(h1n1)-outbreak> accessed 25 November 2021.

Figure 10: Number of patent families by first filing year and by type of patent applicant



Source: Authors' calculations based on VaxPaL data.

Figure 11 demonstrates the first filing dates for the patent families related to each of the four vaccine technology platforms with a view to illuminating of their technological development timelines.

Among the four technology platforms, mRNA vaccine is the latest technology, which are covered by 32 pre-COVID patent families and only one post-COVID patent family. Of the pre-COVID patent families, most (22 of 32) were filed during the period of 2011 to 2016, and three were filed in 2006. The first patent relating to mRNA-based vaccine was filed in 2002, which covers CureVac's RNAactive platform used in the preparation of that company's COVID-19 vaccine (CVnCoV).

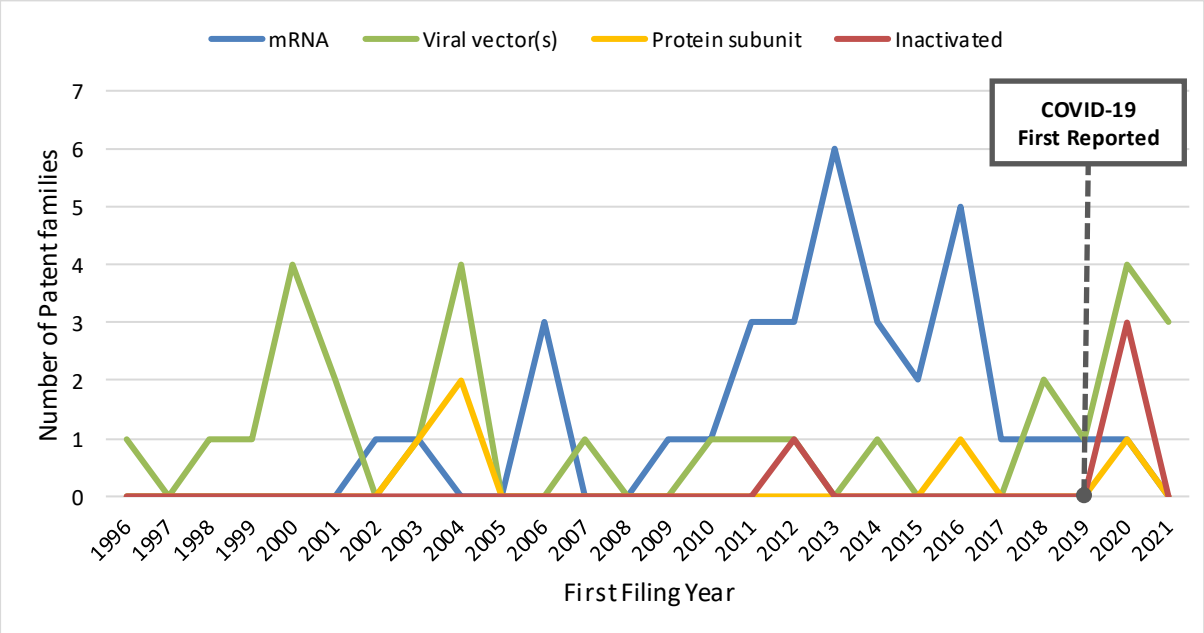
In contrast to mRNA, inactivated vaccine, as the most conventional and well-established technology, is only covered by one pre-COVID patent family filed by the University of Kansa in 2012, and three post-COVID patent families filed in 2020, including one by the Wuhan Institute of Biological Products and two by Sinovac.

There are only five patent families for protein subunit vaccines, all of which were filed by Novavax between 2003 and 2020.

With respect to viral vector vaccine, there are 22 pre-COVID patent families, and seven post-COVID patent families (four filed in 2020 and three in 2021). The earliest patent filing was jointly made by Leiden University and Introgene in 1996, covering the PER.C6 cell line technology used in the preparation of Ad26.COV2-S (J&J) vaccine.[84] Of the 22 pre-COVID patent families, half were filed between 2000 to 2004.

[84] JanssenMD, 'Janssen COVID-19 Vaccine' (27 August 2021) <www.janssenmd.com/janssen-covid19-vaccine/product-properties/product-technology/advac-and-perc6-technology-of-the-janssen-covid19-vaccine> accessed 10 October 2021.

Figure 11: Number of patent families by first filing year and by type of technology platform



Source: Authors' calculations based on VaxPaL data.

Several COVID-19 vaccines, particularly those based on mRNA, were developed within less than one year, widely considered as unprecedented in vaccine development history. However, an overwhelming part of these vaccines deployed patented pre-COVID technologies, as indicated in Figure 9. One typical example is the very first mRNA-based vaccine, BNT162b2 (Pfizer/BioNTech) based on a series of patent families, the first of which was filed by Protiva as early as in 2003.

In addition, there is an evident peak of patent filing by private enterprises and public research institutions with a focus on viral vector and inactivated vaccine technologies in 2020 and 2021. According to the above-mentioned association between the outbreak of SARS, MERS, and Ebola and subsequent patent filing peaks, it is likely that the number of post-COVID patent filings will increase when more patent filing information is published in the course of 2022.[85]

5.4 Patenting activity by office of first filing (OFF)

This section investigates offices of first filing (OFF) of the 74 patent families related to the ten selected COVID-19 vaccines.

OFF means the first patent office where an applicant files a patent application for a specific invention. In theory, an applicant can file an application with any national or regional patent office, or with WIPO in accordance with the PCT. In practice, many applicants choose to file applications in their country of residence at first and then decide whether to file an international application for patent protection in other countries.

OFF data can therefore be used as an indicator of countries of origin of vaccine innovations, thus helping understand geographical distribution of COVID-19 vaccine innovation activities. Meanwhile, it is likely that those originating countries, as sources of vaccine technology, will experience an outflow of patented innovations to other countries.

In this paper, the OFFs of these patent families are discerned from the filing numbers of the priority applications being claimed.[86] For example, "WO 2012/172277" is the PCT publication number of one

[85] COVID-19 vaccine innovation started in 2020, and corresponding patent applications are likely filed in 2021. Given that patent applications are generally published 18 months after their first filing, these patent applications may only be published after mid-2022.

[86] WIPO, 'Numbering of applications and priority applications – Current practice' (September 2017) <www.wipo.int/export/sites/www/standards/en/pdf/07-02-06.pdf> accessed 12 October 2021.

patent family covering AZD1222 (AstraZeneca/Oxford).[87] According to its priority application number "GB 1108879" and WIPO country code for the United Kingdom (GB), this patent is discerned as first filed in the United Kingdom.

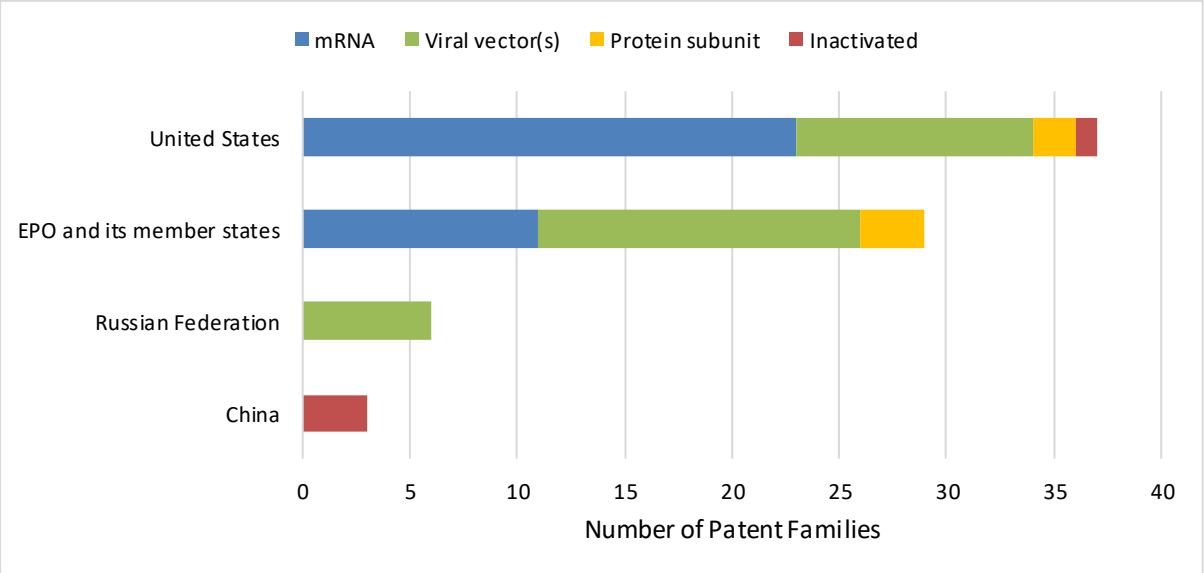
Of the 74 patent families, 73 patent families were filed in one OFF while one patent family was filed in two OFFs simultaneously, namely USPTO and the EPO. As Figure 12 demonstrates, of these 73 patent families, almost half (36) were first filed in the United States, and more than one third (28) were first filed before the EPO and/or national patent offices of EPO member states.[88] Of the remaining nine, three were filed in China and six in the Russian Federation.

While one vaccine, Covaxin, was developed in India by Bharat/ICMR, the patent family related to this vaccine was filed by the Wuhan Institute of Biological Products in China rather than in India. This is another example demonstrating that the linkage between a specific patent family and a vaccine does not necessarily imply any connection between the patent applicant and the vaccine developer.

In terms of the four technology platforms, 34 patent families related to mRNA were first filed in either the United States or Europe. 31 patents in relation to viral vector were filed in OFF separately in Europe (14), the United States (10), Russian Federation (6), and one in both USPTO and EPO, as indicated above. The only protein subunit-based vaccine involves five patent families, which were first filed in the United States (2) and Sweden (3) respectively. China is the OFF of three out of four patent families related to inactivated vaccine.

Most of the above-mentioned countries are among top 25 innovation economies identified in the WIPO Global Innovation Index 2021.[89]

Figure 12: Office of first filing of patent families



Source: Authors' calculations based on VaxPaL data.

As above explained, the OFF is not necessarily the same as country of residence of patent applicants. As of 9 June 2021, 71 out of 74 patent families have already published information on the residence of patent applicants, as depicted in Figure 13. 65 patent families were filed by applicants from the

[87] In the international phase of PCT, the code "WO" denotes an international application filed with any PCT receiving office, and the code "IB" denotes an international application filed with the International Bureau of WIPO as a PCT receiving office. WIPO, 'PCT Applicant's Guide – International Phase – Annex K' (12 September 2019) <www.wipo.int/export/sites/www/pct/guide/en/gdvol1/annexes/annexk/ax_k.pdf>.

[88] It is noted that the United Kingdom is one of the member states of the EPO.

[89] WIPO, *Global Innovation Index 2021: Tracking Innovation through the COVID-19 Crisis* (WIPO 2021). The top 25 innovation economies are Switzerland; Sweden; United States; United Kingdom; Republic of Korea; Netherlands; Finland; Singapore; Denmark; Germany; France; China; Japan; Hong Kong, China; Israel; Canada; Iceland; Austria; Ireland; Norway; Estonia; Belgium; Luxembourg; Czech Republic; and Australia.

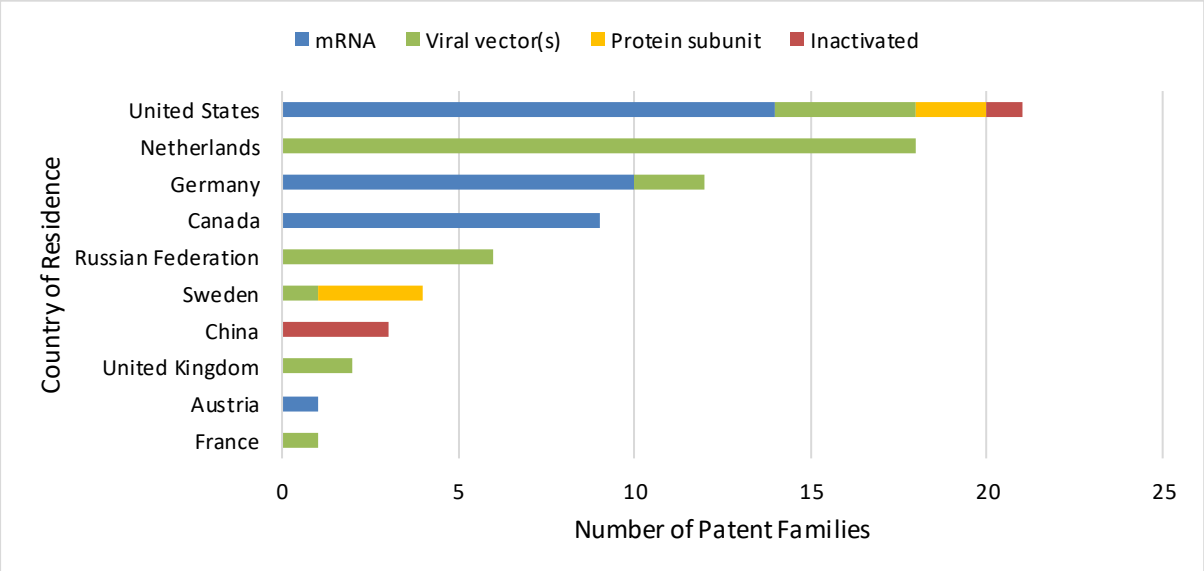
same country. Meanwhile, six were submitted by applicants from more than one country, that is, from Germany and the Netherlands, from Canada and Germany, from France and the Netherlands, from the Netherlands and the United States, and the Netherlands and Sweden respectively. The multiple countries of residence of patent applicants in one patent family indicate that there is cross-country collaboration for vaccine development and patent application.

Of the 71 patent families, 21 patent families have applicants residing in the United States, 18 have applicants from the Netherlands, 12 have applicants from Germany, nine have applicants from Canada, six have applicants from the Russian Federation, four have applicants from Sweden, three have applicants from Austria, China, and France respectively.

Breaking down patenting activity by the four technology platforms, 14 mRNA-related patent families are filed by applicants from the United States, followed by Germany (10), Canada (9) and Austria (1). The Netherlands is the country of residence of most viral vector patent applicants, with 18 out of 31 patent families involving applicants from the country. Other countries, including the Russian Federation (6), United States (4), Germany (2), United Kingdom (2), Sweden (1) and France (1), also host patent applicants of viral vector-related inventions. Applicants of five protein subunit-related patent families are from the United States and Sweden. Two patent families related to inactivated virus involve applicants from the United States and China respectively.

In addition, six out of the ten COVID-19 vaccines involve patent applicants located in multiple countries. These six vaccines are Covaxin (Bharat/ICMR), CVnCoV (CureVac), Ad26.COV2-S (J&J), mRNA-1273 (Moderna), NVX-CoV2373 (Novavax), and BNT162b2 (Pfizer/BioNTech). It once again illustrates that there was extensive cross-country collaboration for COVID-19 vaccine development.

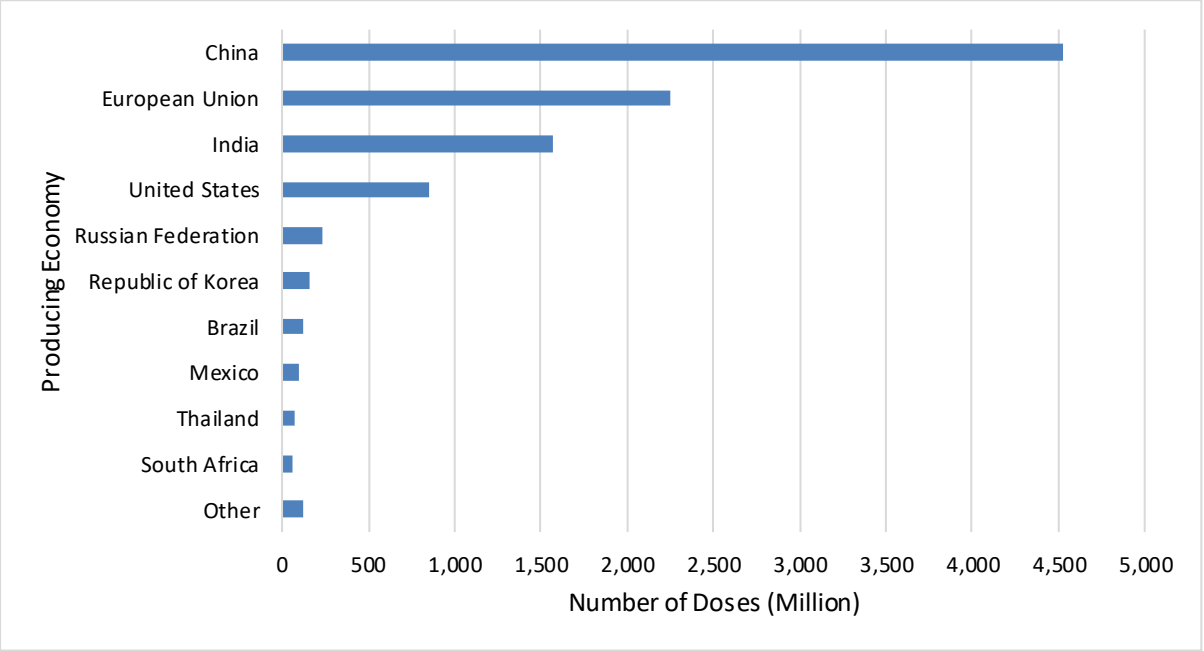
Figure 13: Patent applicant's country of residence



Source: Authors' calculations based on VaxPaL data.

It is interesting to note that the top OFF countries moderately correspond to the countries dominating COVID-19 vaccine production (see Figure 14). For example, top COVID-19 vaccine producing economies, such as China, European Union, the United States, Russian Federation, are the only four receiving first patent filings.

Figure 14: COVID-19 vaccine production by economy (as of 31 December 2021)



Source: WTO-IMF COVID-19 Vaccine Trade Tracker.

5.5 Patenting activity by office of subsequent filing (OSF)

This section describes subsequent patent filing activities related to the 74 patent families, in particular their filing locations.

Given its territorial nature, patent protection only provides exclusive rights for a patented invention within the country or region that grants the patent. Thus, a patent applicant must file its patent application in each of the countries or regions where it wishes to gain patent protection either by filing a local application before national or regional patent office, or by entering the national phase of the patent procedure in that country on the basis of a PCT application, and claim priority based on the date of the application filed at the OFF.

Typically, patent applicants would choose to first file a local application in their country of residence. If they wish to obtain patent protection in other countries, they can file a PCT application within 12 months from the priority date, and then request to enter the national or regional phase in any PCT contracting states within 30 months from the priority date.[90] Alternatively, the patent applicant can submit the application within the regular priority period under the Paris Convention.[91]

Filing a patent application and maintaining a patent entails a certain cost including filing, examination, and maintenance fees; such costs inevitably increase as protection is sought in more jurisdictions entered. The overwhelming majority of patents are not filed or prosecuted in the majority of countries worldwide, especially LMICs (excluding China).[92] Several factors are often considered by patent applicants in their decisions on which country the patent application should be filed.[93] One important factor is whether the country of filing would provide patent applicants with potential market to use their inventions. In other words, the patent applicant must strike a balance between

[90] It should be noted that several subsequent filings are not submitted through the PCT national phase entry route. For example, as shown in Figure 15, Chinese Taipei is not a PCT member, but a patent applicant may still claim priority right based on a PCT application as long as the applicant is from a WTO Member and such PCT application designates this WTO Member as a designated country.

[91] The Paris Convention, art 4.

[92] According to WIPO IP Statistics Data, of 3,276,700 patent applications filed in 2020, about 47% were filed in high-income countries, 46% were filed in China, and only 7% were filed in LMICs (excluding China). WIPO, 'WIPO IP Statistics Data Center' <www3.wipo.int/ipstats/> accessed 15 December 2021.

[93] David Reed, 'National Phase Entry: A User's Perspective' (4 August 2011) <www.wipo.int/export/sites/www/pct/en/pct_strategies/nat_phase_entry_users_perspective.pdf> accessed 10 October 2021.

the costs of filing in a country and their estimate of potential economic returns obtained from the market in that country. A further consideration, apparent in the pharmaceutical sector, is the inherent production capacity in the countries concerned.

Thus, offices of subsequent filing (OSF) of the 74 patent families can help to understand which countries are considered by patent applicants as potential markets for the "use" of their patent technologies.[94] Since the main venue to use a patent is to make patented products or use patented processes, OSF can further indicate the site for potential local production and technology transfer. In other words, the country of OSF may expect an inflow of technologies from the country of the first filing.

Of these 74 patent families, more than 80% (61 out of 74) filed subsequent applications after their first filings, and of these, 59 already entered the national phase in at least one other jurisdiction in addition to the first filing country or region. These subsequent filings are mainly focused on technologies related to mRNA and viral vector platforms, given that the number of patent families related to these two platforms accounts for more than 80% of the 74 patent families.

As of 9 June 2021, 13 patent families related to four technology platforms were not covered by the subsequent applications: six from the United States, three from China, three from the Russian Federation, and one from the EPO. Of these 13 patent families, nine are still within the 12-month priority period from the first filing date, and four did not file subsequent application within the priority period. These 13 patent families are therefore not included in Figure 15.

Top five OSFs for the 61 patent families with subsequent applications are located in the United States, Europe (EPO), Canada, Australia, and Japan as shown in Figure 15. Each has received filings of more than 40 patent families. China, India, and Republic of Korea have also received more than 20 patent families filed before their national patent offices respectively. It is clear that the subsequent patent filing activities of the ten COVID-19 vaccines are highly concentrated in top 25 innovation economies,[95] particularly these hosting the five largest IP offices in the world.[96]

Concerning geographical distribution, North America and Europe are the most popular destinations for subsequent filings, which corresponds to the top regions of origin of vaccine innovative activities as discussed in section 5.4. The Asia-Pacific region, including Australia; China; Hong Kong, China; India; Japan; Republic of Korea; New Zealand; and Singapore, appears to be the third most popular region for subsequent filings. These jurisdictions in the region may either provide large markets or have vaccine manufacturing capacity.[97] While many countries within the Asia-Pacific region have received subsequent filings of patents related to COVID-19 vaccines, only China and India collectively host three vaccine originator companies, i.e. Sinopharm/Beijing, Sinovac, and Bharat/ICMR.

In Latin America and the Caribbean, two countries, namely Brazil and Mexico, have received more than ten patent families' subsequent filings. In Central and Eastern Europe, Central Asia, and

[94] According to Article 28 of the TRIPS Agreement, a patent owner has exclusive rights to prevent third parties from making, using, offering for sale, selling, or importing his patented product; or to prevent third parties from using his patented process and the product obtained directly by that process.

[95] WIPO (n 89).

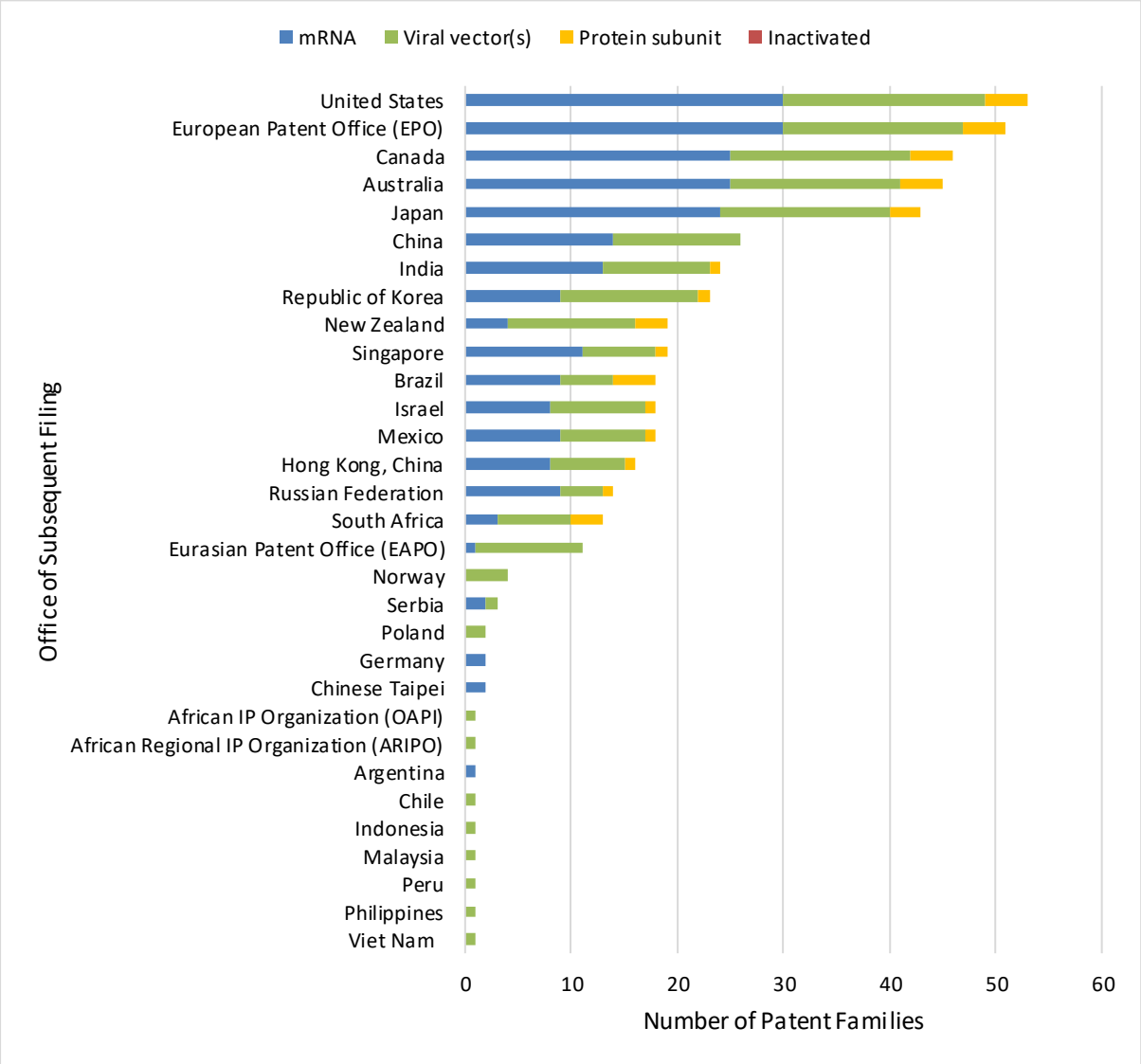
[96] These five patent offices are the US Patent and Trademark Office (USPTO), European Patent Office (EPO), Japan Patent Office (JPO), Korean Intellectual Property Office (KIPO), and National Intellectual Property Administration (CNIPA, formerly SIPO).

[97] For instance, Australia started local production of AZD1222 (AstraZeneca/Oxford) and BNT162b2 (Pfizer/BioNTech) vaccines this year. Christopher Knaus and Nick Evershed, 'Australian Production of AstraZeneca Vaccine in Early July just One-tenth of What Government Promised' *The Guardian* (16 July 2021) <www.theguardian.com/australia-news/2021/jul/16/australian-production-of-astrazeneca-vaccine-in-early-july-just-one-tenth-what-government-promised> accessed 10 October 2021. In the meantime, Japan, Korea, and Singapore are also expanding vaccine manufacturing facilities. Kentaro Iwamoto, 'BioNTech to produce vaccine in Singapore, as It Expands in Asia' *Nikkei Asia* (10 May 2021) <https://asia.nikkei.com/Spotlight/Coronavirus/COVID-vaccines/BioNTech-to-produce-vaccine-in-Singapore-as-it-expands-in-Asia> accessed 10 October 2021. Hyonhee Shin, 'S.Korea pledges nearly $2 bln to become major COVID-19 vaccine producer' *Reuters* (5 August 2021) <www.reuters.com/world/asia-pacific/skoreas-moon-vows-invest-192-bln-by-2025-boost-vaccine-capacity-blue-house-2021-08-05/> accessed 10 October 2021. Reuters Staff, 'Japan's JCR Pharma to build new plant to produce COVID-19 vaccine solution' *Reuter* (4 March 2021) <www.reuters.com/article/us-jcr-pharms-vaccine-plant-idUSKBN2AW0UB> accessed 10 October 2021.

Caucasus region (CEECAC, excluding countries that are EPO member states[98]), Israel is the top destination for subsequent filings, followed by the Russian Federation and Eurasian Patent Office (EAPO).[99] It should be noted that South Africa is the only country in Africa that have received more than ten subsequent filings, including three mRNA-related filings, seven viral vector-related filings and three protein subunit-related filings. Among the 61 patent families, no subsequent filings have been filed in Arab and Middle East region.

In terms of the four technology platforms, none of patent families related to inactivated vaccine has subsequently been filed in other than the office of first filing. The other three technology platforms have at least one subsequent filing. It is interesting to note that viral vector-related patent families have been most widely filed, followed by mRNA and protein subunit-related patent families.

Figure 15: Office of subsequent filing of patent families



Source: Authors' calculations based on VaxPaL data.

[98] North Macedonia, Serbia and Turkey are EPO member states that are located in CEECAC.

[99] EAPO member states are Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, the Russian Federation, Tajikistan, and Turkmenistan. EAPO, 'Eurasian Patent Organization (EAPO)' (2021) <www.eapo.org/en/members.html> accessed 10 October 2021.

5.6 Legal status of patent families by jurisdiction

This section provides a snapshot on the legal status of 74 patents families related to four vaccine technology platforms in various jurisdictions as of 9 June 2021.

Understanding the legal status of these patent families is a crucial step toward a fact-based policy and legislative decision-making process on technology transfer and local production.

In order to visualize the legal status of these 74 patent families, the following world maps use three colours to represent each of the three stages of patent filings relating to a particular vaccine technology platform in each jurisdiction: (1) Granted (red): at least one patent has been granted in the jurisdiction; (2) Pending (yellow): no patent has been granted, but there is at least one patent application pending in the jurisdiction; and (3) Inactive (green): there is neither a granted patent nor a pending patent application, either because the patent application has been withdrawn, lapsed, abandoned or rejected. Jurisdictions in grey are those where no patent application information is available. It should be noted that the unavailability of information does not necessarily indicate an absence of patent application in those jurisdictions.

If one jurisdiction has patents or patent applications falling into more than one of the above-mentioned three coloured categories, the global map records the status of granted patents (red) rather than the status of pending patent applications (yellow) and inactive patent applications (green) in the jurisdiction concerned. Similarly, the status of pending patent applications (yellow) is illustrated rather than the status of inactive patent applications in that jurisdiction. In other words, where there is a mixture of patents or patent applications with differing legal status, the map records the status most relevant to access to technologies.

Furthermore, the gradient of each colour represents the number of patents or patent applications under that legal status. The darker the colour, the more the patents or patent applications have been identified under that status. For example, the United States is coloured with the darkest red in Figure 16, which means that 32 patents linked to mRNA-based vaccines have already been granted in the country.

As of 9 June 2021, 150 patents related to the three mRNA-based vaccines had already been granted in 54 jurisdictions.[100] As shown in Figure 16, 32 patents had been granted in the United States, 20 in Australia, 19 in several EPO member states (legal status may vary by jurisdiction), 18 in Japan, ten in China, eight in the Russian Federation, six in Canada, Israel, and Mexico respectively, five in the Republic of Korea and Singapore respectively, four in Hong Kong, China; India; and New Zealand respectively, and three in South Africa. In addition, eight applications were pending in Brazil, one was pending in each of the EAPO member states (except for the Russian Federation), and one in the Republic of Moldova.[101]

No granted patents or pending applications related to mRNA technology was identified in Chinese Taipei despite the fact that two mRNA-related applications had been filed: one was rejected and the other was withdrawn. In Argentina, one patent application was filed and subsequently abandoned.

Concerning other countries, mostly located in Africa, Latin America, Middle East, and Southeast Asia, coloured in grey, there is no information indicating that they have received any mRNA vaccine-related patent applications.

In comparison with mRNA vaccine technologies, patents related to the three viral vector-based vaccines appear to be granted more widely. As shown in Figure 17, there are 95 patents being granted in 102 jurisdictions, including the Russian Federation (10); United States (9); Australia (7); China (7); most of the EPO member states (1-7 patents granted, varying by country); Japan (6);

[100] Rule 13.1 of the PCT Regulations provides "The international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ('requirement of unity of invention')", and therefore after entering national phase, a PCT application may be split into multiple national patent applications according to national patent law. Additionally, as of 9 June 2021, the technical information on several vaccines is not yet available, and thus a small number of patents whose relevance with the vaccines requires further assessment will be excluded from the discussions in this section.

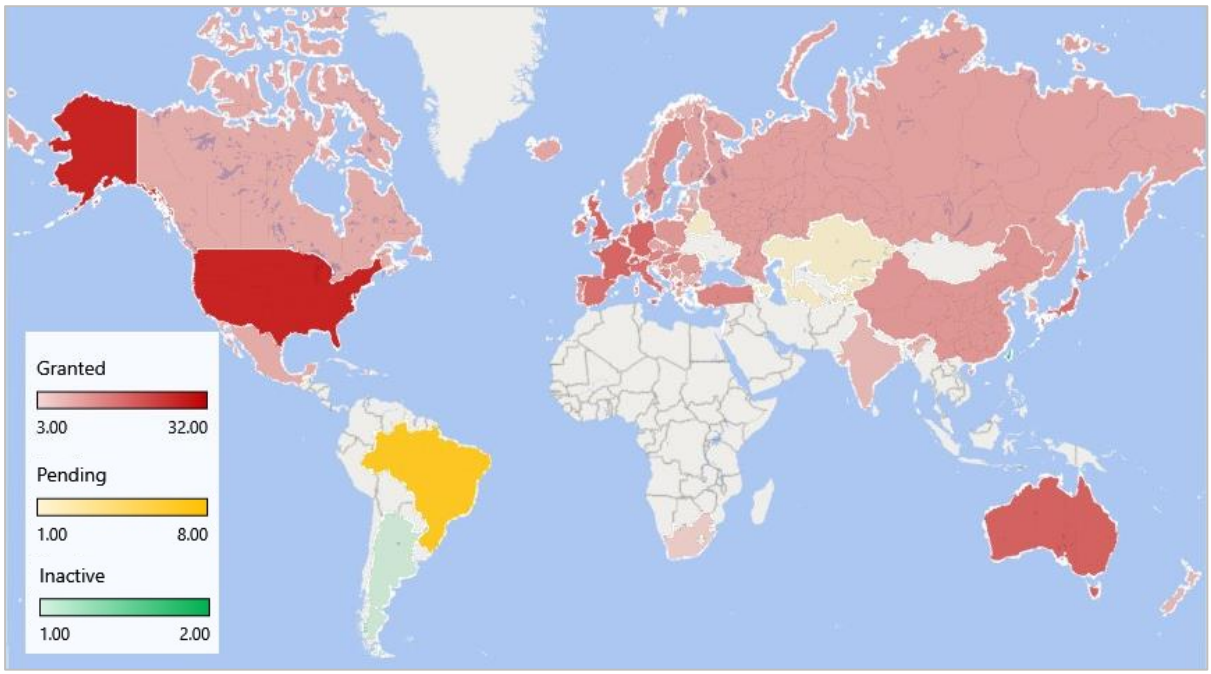
[101] The Republic of Moldova signed a validation agreement with the EPO in 2015. EPO, 'Validation agreement with the Republic of Moldova enters into force' (1 November 2015) <www.epo.org/news-events/news/2015/20151101.html> accessed 18 November 2021.

South Africa (6); Hong Kong, China (5); India (5); Republic of Korea (5); Canada (4); Israel (4); New Zealand (4); Singapore (4); and Mexico (3). In addition, EAPO member states (3-6 patents granted, varying by country), Republic of Moldova (3), Brazil (2), African Intellectual Property Organization (OAPI) (1), African Regional Intellectual Property Organization (ARIPO) (1), Malaysia (1), the Philippines (1), Viet Nam (1) have also granted patents related to this technology platform respectively. One patent application that has led to granted patents in most of these above-mentioned jurisdictions is Crucell's PCT publication number WO 2015/040002 A1, while its national phase applications are still pending in a few countries, including Chile, Indonesia, and Peru, as highlighted in yellow on the map.

As shown in Figure 18, 25 patents involved in NVX-CoV2373 (Novavax) have been granted in 22 jurisdictions, including the United States (5), Australia (3), Canada (3), Japan (3), New Zealand (3), South Africa (3), Brazil (2), most of the EPO member states (1-2 patents granted), and Russian Federation (1). While other countries have not granted patents yet, many of them have received patent applications related to this protein subunit-based vaccine, including several EPO member states; China; Hong Kong, China; India; Israel; Mexico; Republic of Korea; and Singapore.

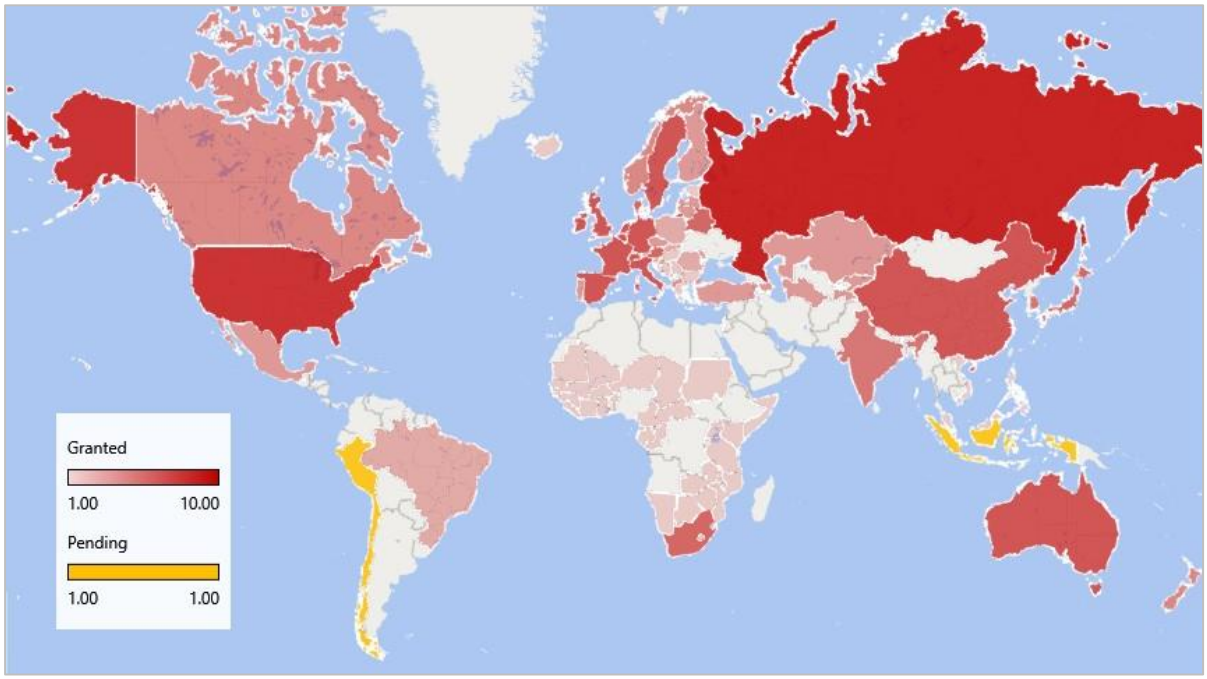
As shown in Figure 19, of the four patent families related to the three inactivated whole virus vaccines, only one has been granted in the United States, and the other three applications filed in 2020 are still pending in China. There is no information on whether other countries have received patent applications related to these inactivated vaccines.

Figure 16: Patent status of mRNA-based vaccines in WTO Members



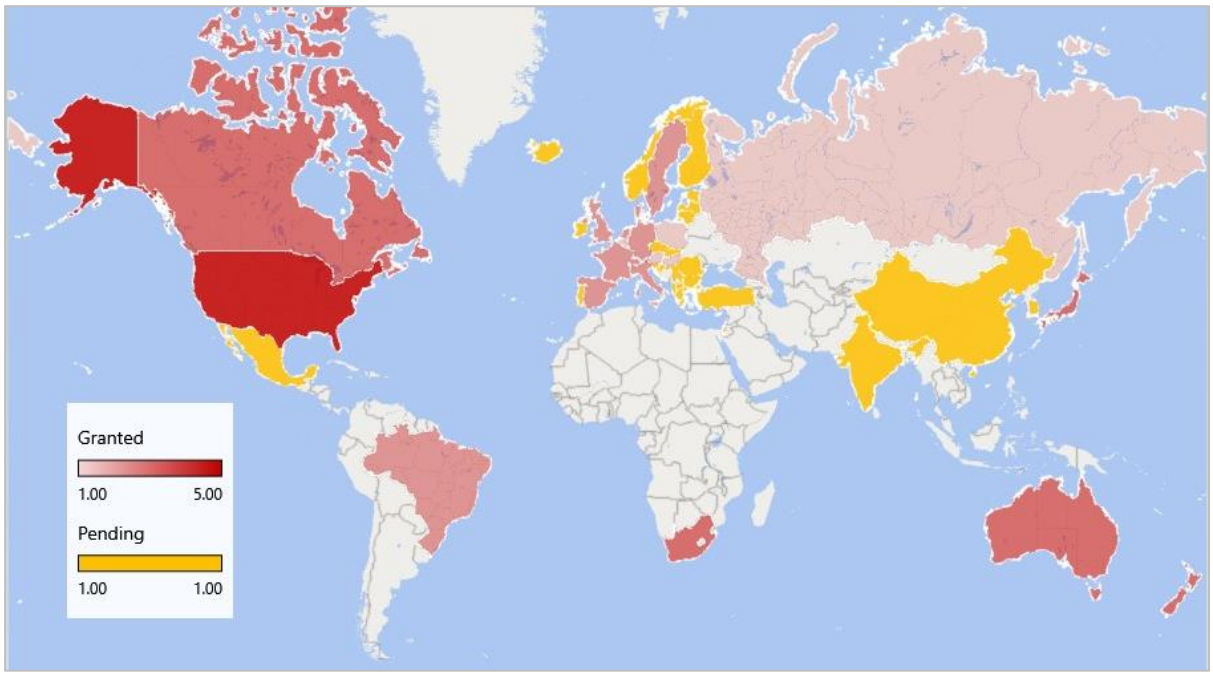
Source: Authors' calculations based on VaxPaL data.

Figure 17: Patent status of viral vector-based vaccines in WTO Members



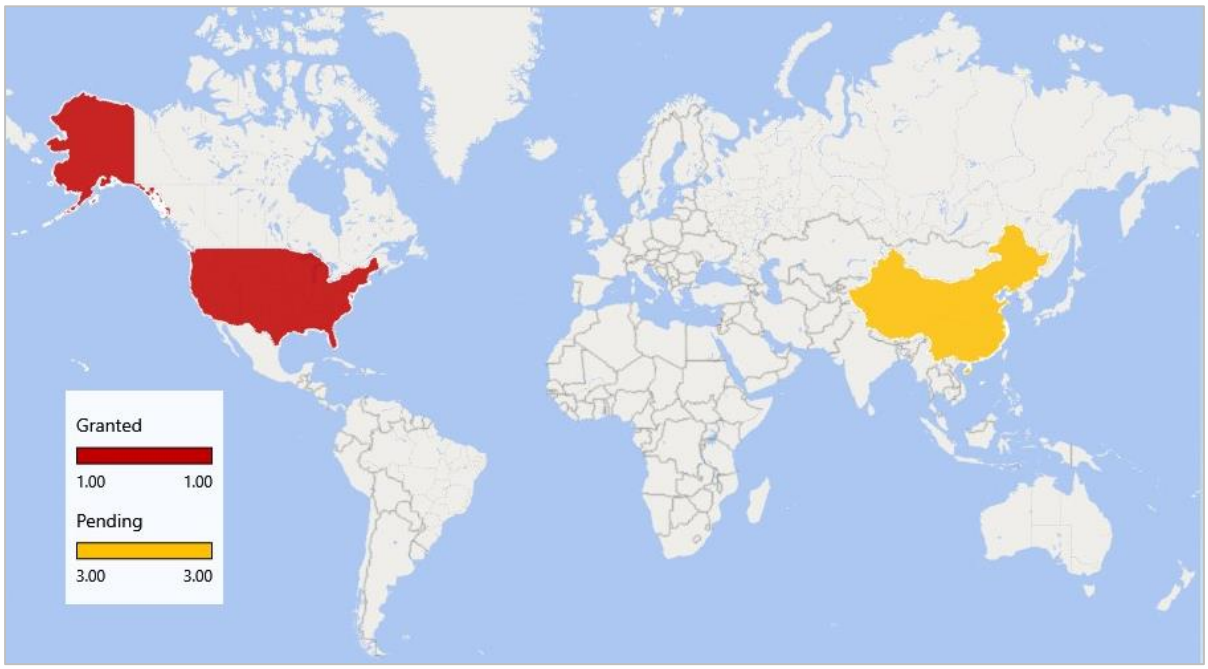
Source: Authors' calculations based on VaxPaL data.

Figure 18: Patent status of protein subunit-based vaccines in WTO Members



Source: Authors' calculations based on VaxPaL data.

Figure 19: Patent status of inactivated vaccines in WTO Members



Source: Authors' calculations based on VaxPaL data.

6 KEY FINDINGS

Through the statistical and analytical review of the 74 patent families related to the ten COVID-19 vaccines reported in VaxPaL, several key findings can be summarized as follows:

Patent intensity: There are wide variations in the number of patent families involved in each COVID-19 vaccine, reflecting the different technology platforms deployed for vaccine development. Each of four technology platforms has its own advantages and disadvantages. In general, mRNA and viral vector-based vaccines are more patent-intensive than whole virus and protein subunit-based vaccines. Nevertheless, there is different patent intensiveness even between the vaccines based on the same technology platform. mRNA, as the most patent-intensive technology platform, involves several patent families covering technologies that are utilized by a number of vaccines, and its patent landscape is very complex and dynamic.

Nature of patent applicant: The review of patenting trends highlights a major role on the part of private enterprises in COVID-19 vaccine innovation and development, while suggesting that public research institutions and universities have largely made their contributions through conducting basic scientific research. Research collaboration among different sectors has proven to be important and essential in the COVID-19 vaccine development process. In addition to their own R&D investment, private enterprises have received a significant amount of external funding for their vaccine development. Among these private enterprises, it is SME biotech companies rather than traditional large vaccine companies that have made substantive contributions to COVID-19 vaccine development, particularly in the early development stage.

Timeline of patent filing: Patenting activities of the 74 patent families spread from 1996 to 2021, and most patent applications were filed before December 2019. Given that the term of patent protection is normally 20 years from the first filing date, seven patent families had already expired at the end of 2020, and two other patent families are expected to expire by the end of 2021. Regarding patent families filed after December 2019, there is a distinct peak of filings by private enterprises and public research institutions during the period from 2020 to 2021, and the filings are mainly focused on viral vector and inactivated vaccine technologies. Thus, the successful development of COVID-19 vaccines benefits from years of medical research and development efforts made by numerous scientists and researchers worldwide before and after the outbreak of the COVID-19 pandemic.

Office of first filing: Of the 74 patent families, almost half were first filed in the United States, more than one third were first filed in Europe, and only three and six were first filed in China and the Russian Federation respectively. The first filings in the United States and Europe were mainly focused on mRNA and viral vector-related technologies, while the first filings in China and the Russian Federation were on inactivated virus and viral vector-related technology respectively. COVID-19 vaccine innovation activities, particularly mRNA-related innovation, mainly took place in the United States and Europe, which demonstrates their long-standing technical strengths in the pharmaceutical and biotechnology industries.

Office of subsequent filing: More than three fourths of the 74 patent families, mainly focused on mRNA and viral vector-related technologies, have subsequent filings in other jurisdictions. The top destinations of these subsequent filings are North America (Canada and United States), Europe (EPO member states), and Asia-Pacific (including Australia; China; Hong Kong, China; India; Japan; Republic of Korea; and Singapore). In Latin America and the Caribbean, only two countries (Brazil and Mexico) received more than ten subsequent filings. In the CEECAC region, Israel, Russian Federation, and the Eurasian Patent Office (EAPO) are destinations for subsequent filings. South Africa is the only country in Africa receiving more than ten subsequent filings.

Legal status of patent families in WTO Members: 150 patents related to mRNA vaccines have already been granted in 54 jurisdictions, mainly in North America (Canada and United States), Europe (EPO member states), the Asia-Pacific (Australia; China; Hong Kong, China; India; Japan; Republic of Korea; Singapore; and New Zealand), the CEECAC region (Israel and Russian Federation), and Latin America (Mexico) and Africa (South Africa). A few patent applications are still pending, while others have been either withdrawn, rejected, or abandoned in several jurisdictions. There is no information on whether some jurisdictions in Africa, Latin America, Middle East, and Southeast Asia have received any mRNA vaccine-related patent applications.

In comparison with mRNA, patent families related to viral vector-based vaccines appear to be granted more widely. 95 patents have been granted in 102 jurisdictions, namely in North America (Canada and United States), Europe (EPO member states), Asia-Pacific (including Australia; China; Hong Kong, China; India; Japan; Republic of Korea; Malaysia; New Zealand; the Philippines; Singapore; and Viet Nam), CEECAC (EAPO member states, including Israel; Republic of Moldova; Russian Federation), Africa (African Intellectual Property Organization (OAPI), African Regional Intellectual Property Organization (ARIPO), South Africa), and Latin America (Brazil).

For protein subunit vaccines, 25 patents were granted in 22 jurisdictions, including the United States, Australia, Canada, Japan, New Zealand, South Africa, Brazil, EPO member states, and Russian Federation. Several other EPO member states; China; Hong Kong, China; India; Israel; Republic of Korea; Mexico; and Singapore received the applications but have not yet issued their office actions.

Regarding inactivated virus-related vaccines, only one patent has been granted in the United States, and three patent applications have been filed in 2020 in China.

These key findings illustrate that the legal status of the 74 patent families involved in the ten COVID-19 vaccines is highly divergent across the different jurisdictions. There is no such thing as an "international patent" or "COVID-19 vaccine patent", nor a one-on-one correspondence between any current vaccine and one specific patent. Country-level analysis of the legal status of these 74 patent families is ultimately essential for national policy and decision makers to make evidence-based holistic national and regional policies in order to promote technology transfer and strengthen local production capacity. A clear understanding of the legal status of patents and patent applications in distinct jurisdictions is also crucial to inform the ongoing policy debate on the role of IP rights in the promotion of technology transfer and local production. It may contribute to identifying potential IP-related obstacles to local production, to developing corresponding IP strategies to address any identified obstacles, and more broadly, to making well-informed technology and public health policies and legislative decisions in response to the COVID-19 crisis and future pandemics.

It should be reiterated that the above-mentioned key findings are based on the analysis of the VaxPaL data released on 9 June 2021. Since the development of COVID-19 vaccines and the patent data relating to these vaccines are highly dynamic, these findings are subject to review and update in the future.

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