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Technology Transfer for Production of COVID-19 Vaccines in Latin America*

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Latin American and Caribbean (LAC) countries were severely hit by the COVID-19 pandemic.[1] As of April 2021, the region was reported to have experienced nearly 30 percent of the world's COVID-19 deaths, despite accounting for less than 10 percent of the population.[2] The devastation continued through 2021, a period when vaccines had been approved, but access to these essential products remained limited. National vaccination campaigns in many LAC countries were slow to take off, allowing illness and death rates to soar. While LAC countries' estimated number of cumulative excess deaths per million people was 100 at the end of 2020, this increased to over 300 by October 2021 as Figure 15.1 shows.

Although restricted access to vaccines in 2021 was due to multiple factors (and, of course, death rates are attributable to more than access to vaccines), many observers came to link the dire effects of COVID-19 to the region's dependence on imported vaccines that were in scarce supply. Vaccination in LAC countries relied mostly on purchases from the World Health Organization's (WHO) joint procurement facility,

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1 *Four Perspectives on Pandemic Severity* (2021), https://pandem-ic.com/four-perspectives-on-pandemic-severity/ (last visited Dec. 6, 2022); Juan Grigera, *Adding Insult to Injury: The COVID-19 Crisis Strikes Latin America*, 53 DEV. CHANGE 1335 (2022); Jorge LaRotta et al., *COVID-19 in Latin America: A Snapshot in Time and the Road Ahead*, 12 INFECT. DIS. THER. 389 (2023).

2 Adam Jourdan & Adam Jourdan, *Latin America's Vaccine Shortage Threatens Fragile Revival as Pandemic Rages*, REUTERS (Apr. 26, 2021), www.reuters.com/world/americas/latin-americas-vaccine-shortage-threatens-fragile-revival-pandemic-rages-2021-04-26/ (last visited Dec 6, 2022); Nicolò Gozzi et al., *Estimating the Impact of COVID-19 Vaccine Inequities: A Modeling Study*, 14 NAT. COMMUN. 3272 (2023).

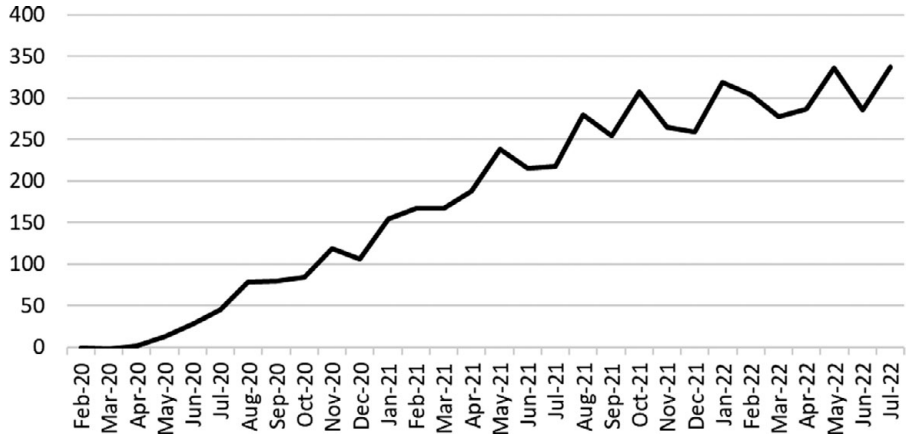

FIGURE 15.1 Cumulative excess mortality in Latin America and the Caribbean (per million people)
Excess deaths are calculated as the number of all-cause deaths minus the number of deaths expected for the same period based on previous data, per million people. The data in the figure are cumulative, relative to the baseline of January 2020. Although Our World in Data includes Mexico as part of "North America," the data used for the figure are based on a recalculation with Mexico included as part of LAC. Note that I report LAC alone, and not inter-regional comparisons, because high levels of missing data from other regions make such comparisons unreliable.
Source: Our World in Data (https://ourworldindata.org/excess-mortality-covid).

COVAX,[3] and directly from vaccine manufacturers. A common diagnosis that emerged is that more local or regional production of vaccines could have ameliorated the impact of the pandemic – and local production has subsequently come to be regarded as a way to assure that what transpired in the COVID-19 pandemic is not repeated during future health emergencies. To that end, regional organizations and many national governments embarked on strategies to increase local production.[4] As the authors of a report by the United Nation's Economic Commission for

[3] COVAX Explained, www.gavi.org/vaccineswork/covax-explained (last visited Dec. 4, 2020).
[4] ECLAC, *Plan for Self-sufficiency in Health Matters in Latin America and the Caribbean: Lines of Action and Proposals*, 98 (2021), www.cepal.org/en/publications/47253-plan-self-sufficiency-health-matters-latin-america-and-caribbean-lines-action-and#:~:text=The%20Plan%20for%20self%2Dsufficiency,and%20medicines%20in%20the%20region (last visited Dec. 7, 2022); PAHO, *Increasing Production Capacity for Essential Medicines and Health Technologies* (2021), www.paho.org/en/documents/cd598-increasing-production-capacity-essential-medicines-and-health-technologies (last visited Dec. 7, 2022); *PAHO Launches New Collaborative Platform to Produce COVID-19 Vaccines in Latin America and the Caribbean*, PAHO/WHO | Pan American Health Organization, www.paho.org/en/news/1-9-2021-paho-launches-new-collaborative-platform-produce-covid-19-vaccines-latin-america-and (last visited Dec. 7, 2022); PROSUR, *Conozca Más Sobre el Proyecto de Escalamiento de Capacidades de Inmunización* (2021), https://foroprosur.org/conozca-mas-sobre-el-proyecto-de-escalamiento-de-capacidades-de-inmunizacion/ (last visited Dec. 7, 2022).

Latin America and the Caribbean on "self-sufficiency" put it, "while the pandemic has laid bare the health vulnerabilities of the region, it has also been an opportunity to re-evaluate its productive and technological capacities, and to reformulate strategies and policies for strengthening local manufacturing and innovation systems for components of goods and services linked to the health complex."[5]

The reckoning that occurred throughout Latin America and the Caribbean is hardly specific to this region.[6] Dependence on – and lack of access to – imported vaccines was acute in Africa as well, and similar diagnoses and proposals have followed.[7] Indeed, the WHO links differences in health outcomes and access to vaccines globally to uneven production patterns,[8] and throughout the world (including in wealthy countries[9]), vulnerabilities revealed by the pandemic are motivating actions to increase production capabilities.[10]

This chapter looks forward by looking back, examining the production of COVID-19 vaccines in the LAC region. The focus is on technology transfer for local production. That is, while efforts to produce original, "home-grown" vaccines are discussed, attention is primarily directed at the extent (or absence) of production in LAC countries of the leading vaccines that were most used internationally, such as those made by AstraZeneca, BioNTech/Pfizer, the Chinese firms Sinopharm and Sinovac, as well as Johnson & Johnson (J&J), Moderna, and Russia's Sputnik-V. The research reveals a limited degree of local vaccine production during the pandemic, what can be regarded as an under-utilization of the region's pharmaceutical production capabilities.

[5] ECLAC, *supra* note 4, at 9.

[6] Nor is acknowledgement of health vulnerabilities as being rooted in industrial weaknesses new to Latin America. Kenneth C. Shadlen & Elize Massard da Fonseca, *Health Policy as Industrial Policy Brazil in Comparative Perspective*, 41 Polit. Soc. 561 (2013).

[7] Sara Jerving, *AU Launches Partnership for African Vaccine Manufacturing*, Devex (2021), www.devex.com/news/sponsored/au-launches-partnership-for-african-vaccine-manufacturing-99654 (last visited Dec. 8, 2022); Victor J. Dzau, Celynne A. Balatbat & Anaeze C. Offodile, *Closing the Global Vaccine Equity Gap: Equitably Distributed Manufacturing*, 399 Lancet Lond. Engl. 1924 (2022).

[8] WHO, *Global Vaccine Market Report 2022* (2022), www.who.int/publications/m/item/global-vaccine-market-report-2022 (last visited Dec. 7, 2022). *See also* Domestic Vaccine Manufacturing Pays Off (2022), https://pandem-ic.com/domestic-vaccine-manufacturing-pays-off/ (last visited Dec. 7, 2022).

[9] National Academy of Medicine, Globally Resilient Supply Chains for Seasonal and Pandemic Influenza Vaccines (2022), https://nap.nationalacademies.org/catalog/26285/globally-resilient-supply-chains-for-seasonal-and-pandemic-influenza-vaccines (last visited Jul. 21, 2022).

[10] To that end, in February 2022 the WHO announced the establishment of an advanced training hub to build national capabilities for the production of vaccines and other biologic pharmaceutical products. WHO, "Moving Forward on Goal to Boost Local Pharmaceutical Production. WHO Establishes Global Biomanufacturing Training Hub in Republic of Korea," www.who.int/news/item/23-02-2022-moving-forward-on-goal-to-boost-local-pharmaceutical-production-who-establishes-global-biomanufacturing-training-hub-in-republic-of-korea (last visited Dec. 8, 2022).

Through the analysis of the technology transfer initiatives, as well as the accompanying regulatory challenges, the chapter sheds light on the intense challenges involved with pandemic vaccine production in the Global South. The analysis also shows, however, that relaxing intellectual property rights to enable "independent" production would not be feasible either, and thus suggests we orient attention to factors that are likely to make partnerships and technology transfer more common.

The chapter proceeds as follows. Section 1 presents an overview of the universe of local production arrangements for which information is publicly available. Section 2 then drills down to the cases where technology transfer advanced the furthest, examining the production experiences of the AstraZeneca vaccine in Brazil and jointly in Argentina and Mexico. Both partnerships illustrate the challenges of building and sustaining supply chains during the pandemic. The Brazil case highlights key steps that enabled relative success, including rapid and proactive efforts by public sector institutions. The Argentina–Mexico case, which appeared to be both more ambitious and better positioned from the start but did not yield the same outcome, sheds light on the technological and regulatory obstacles that may confound such projects. Section 3 provides a broader view of the experience of technology transfer during the pandemic, considering the role of intellectual property rights and pointing to the collaborative dimensions of production partnerships. Section 4 synthesizes the main findings and points to avenues for future research.

To be sure, with LAC vaccination rates among the highest in the world by 2023, the issues discussed in this chapter may no longer appear to be pressing. But building local and regional production capabilities – and making more use of existing capabilities – has important implications for preparedness for future pandemics.[11]

1 COVID-19 VACCINE PRODUCTION IN LATIN AMERICA: OVERVIEW

COVID-19 vaccines can be distinguished among four types: viral vector, inactivated virus, mRNA, and protein-based. While inactivated virus and protein-based vaccines are traditional technologies that have long been used, viral vector and mRNA are both newer platform technologies that involve insertion of genetic code into delivery vessels.[12] Table 15.1 presents the landscape of production partnerships in Latin America and the Caribbean by type of vaccine, and also according to the different stages of the production processes that are being executed locally. Firms may

[11] And potentially for this one, if the need were to emerge to produce new vaccines against resistant variants, for example.

[12] Mariagrazia Pizza, Simone Pecetta & Rino Rappuoli, *Vaccines 2020: The Era of the Digital Vaccine Is Here*, 13 Sci. Transl. Med. eabm3249 (2021). Prior to the COVID-19 pandemic, the only viral vector vaccines approved for human use were for Ebola, and there were no vaccines (or any approved pharmaceutical products) based on mRNA technology.

TABLE 15.1 *Production partnerships: COVID-19 vaccines in Latin America*

Vaccine	Technological platform	LAC country (firm) with partner for drug substance production[a]	LAC country (firm) with partner for fill–finish production[a]
AstraZeneca	Viral vector	Argentina (mAbxience) *Brazil (BioManguinhos)*	*Brazil (BioManguinhos)* Mexico (Liomont)
Sputnik-V	Viral vector		Argentina (Richmond) Brazil (União Química)
CanSino	Viral vector	–	Argentina (Richmond)[b] Mexico (DrugMex)
Johnson & Johnson	Viral vector	–	–
Sinopharm	Inactivated virus	–	–
Sinovac	Inactivated virus	–	*Brazil (Butantan)*
BioNTech/ Pfizer	mRNA	–	Brazil (Eurofarma)[b]
Moderna	mRNA	–	–
Novavax	Protein-based	–	–
Sanofi/GSK	Protein-based	–	–
Corbevax	Protein-based	–	–

[a] Italics indicates the local partner is a publicly owned laboratory.
[b] Late announcements, for eventual, future production.
The partnerships in the table have recorded output or, where indicated, are confirmed agreements for eventual production. Additional reported partnerships are discussed in the text.
Source: Author's compilation from press reports; ECLAC, *Plan for Self-sufficiency in Health Matters in Latin America and the Caribbean: Lines of Action and Proposals*, 98 (2021), www.cepal.org/en/publications/47253-plan-self-sufficiency-health-matters-latin-america-and-caribbean-lines-action-and#:~:text=The%20Plan%20for%20self%2Dsufficiency,and%20medicines%20in%20the%20region; Veronica Vargas, *Analysis of Regional Capacity for Research, Development, and Manufacturing of Vaccines in Latin America and the Caribbean*, Unpublished manuscript, Inter-American Development Bank (2020).

manufacture the "drug substance," which is the core of the vaccine (sometimes referred to as the "antigen"), or they may manufacture the final product that is administered to humans, a stage referred to as "fill–finish" that consists of formulating the drug substance and putting the formulated versions of the vaccine into sterile vials that can be distributed for use.[13] The table shows partnerships for production of five different vaccines across three technological platforms, involving a mix of public and private firms. Manufacturing activities consist mainly of fill–finish, with limited drug substance production. The remainder of this section provides brief overviews, by technological platform.

[13] The upstream and downstream stages of drug substance and fill–finish are the vaccine analogs to producing active pharmaceutical ingredients (API) and final-product formulation for ordinary pharmaceuticals.

A *Viral Vector*

The most important instances of technology transfer for production in the LAC region have been for the AstraZeneca viral vector vaccine, which featured a pair of regional supply chains. The first, announced in June 2020, was with BioManguinhos, a public laboratory in Rio de Janeiro, Brazil, that is linked to the Ministry of Health. BioManguinhos would start by importing the drug substance from AstraZeneca to undertake fill–finish locally, and then in a second phase move to full production with fill–finish operations based on drug substance that it produced too. To supply the rest of Latin America and the Caribbean (excluding Brazil), in August 2020 AstraZeneca partnered with a pair of private firms in Argentina and Mexico to jointly produce the full vaccine, with the drug substance to be made in Argentina and the fill–finish completed by the partner in Mexico. The two AstraZeneca partnerships are discussed in detail in Section 2.

Though limited relative to AstraZeneca, two other viral vector vaccines with local production in the region are CanSino (China) and Sputnik-V (Russia). The main CanSino agreement in the region is in Mexico, with DrugMex, a local firm that was contracted to import the drug substance and produce the final product (that is, execute fill–finish) locally.[14] CanSino also reached an agreement with a private Brazilian firm, Biomm, for local distribution of the vaccine, pending its approval by the national regulator, reportedly with "potential" production in a facility in the state of Minas Gerais.[15] Yet this aspect of the agreement never went beyond potential: CanSino's application for authorization of its vaccine in Brazil listed Biomm as its local representative and distributor, not a producer.[16]

Production agreements for Sputnik-V were established with partners in Argentina and Brazil. In Argentina, Richmond was responding to high demand for this vaccine, aiming to help the Ministry of Health secure more doses in the context of scarce global supply. Argentina was the third country to authorize Sputnik-V, in December 2020, following Russia and Belarus, and the vaccine played an important role in the early stages of Argentina's vaccination strategy.[17] Richmond began with

[14] The first locally completed doses of CanSino were made available in March 2021. Secretaría de Relaciones Exteriores, *The First COVID-19 Vaccines Packaged in Mexico Leave the Drugmex Plant* (Mar. 22, 2021), www.gob.mx/sre/prensa/the-first-covid-19-vaccines-packaged-in-mexico-leave-the-drugmex-plant (last visited Dec. 6, 2022).

[15] Brazil's Biomm Signs Deals to Distribute CanSino COVID-19 Vaccine, Reuters (Oct. 1, 2021), www.reuters.com/world/americas/brazils-biomm-signs-deals-distribute-cansino-covid-19-vaccine-2021-10-01/ (last visited Dec. 6, 2022).

[16] *China's CanSino Requests Emergency Use Approval for Vaccine in Brazil*, Reuters (Nov. 10, 2021), www.reuters.com/business/healthcare-pharmaceuticals/chinas-cansino-requests-emergency-use-approval-vaccine-brazil-2021-11-10/ (last visited Dec. 6, 2022).

[17] According to data from Airfinity, Sputnik-V accounts for approximately 20 percent of the vaccines that were administered in Argentina throughout the pandemic. Its peak usage was in the first half of 2021, where the Sputnik share was two-thirds at the end of March 2021 and still over 50 percent at the end of May 2021.

fill–finish, relying on drug substance imported from Russia.[18] Although Richmond planned an eventual move to drug substance production too, and began construction of a new plant to be able to participate eventually in upstream activities, by the middle of 2022 the Ministry of Health was no longer purchasing and administering Sputnik-V, and local production of the vaccine ceased. At the end of 2022 Richmond announced termination of the collaboration with Sputnik-V and that its new facilities would be used instead to produce products jointly with CanSino, including, potentially, COVID-19 vaccines.[19]

In Brazil, União Química had capacity to produce 8 million doses per month, expecting to use its existing plants in Brasília and São Paulo to manufacture the drug substance and undertake the fill–finish operations, respectively.[20] Yet demand for Sputnik-V in Brazil never matched that in Argentina, as the vaccine had a complicated registration process and was only authorized for use in a limited number of states.[21] Although some Sputnik was exported from Brazil, these were locally finished doses based on imported drug substance.[22] It remains unclear how much (if any) of the drug substance was produced locally. Although a technology transfer team visited União Química's Brasília factory, Airfinity does not record any drug substance output of this vaccine from Brazil.[23]

While other agreements for Sputnik-V production were announced, the announcements tended to be accompanied with minimal information and followed by little action. In Mexico, for example, an agreement was reached in mid-2021 for

[18] Cristina Kroll, *Richmond Fabricará la Sputnik V, Acuerdo*, PharmaBiz.net (2021), www.pharmabiz.net/richmond-fabricara-la-sputnik-v-acuerdo/ (last visited Dec. 6, 2022); *In Latin American First, Argentina to Produce Russia's Sputnik V Vaccine*, France 24 (Apr. 20, 2021), www.france24.com/en/live-news/20210420-in-latin-american-first-argentina-to-produce-russia-s-sputnik-v-vaccine (last visited Dec. 6, 2022).

[19] Christian Atance, *Richmond Cerró Deal con CanSino, Vacunas*, PharmaBiz.net (2022), www.pharmabiz.net/richmond-cerro-deal-con-cansino-vacunas/ (last visited Dec. 6, 2022); *Un Laboratorio Argentino Firma con CanSino Biologics. "Sale Rusia, entra China,"* AgendAR (2022), https://agendarweb.com.ar/2022/10/07/un-laboratorio-argentino-firma-con-cansino-biologics-sale-rusia-entra-china/ (last visited Dec. 6, 2022).

[20] ECLAC, *supra* note 4, at 75. *See also*, from early 2021, Marcelo de Valécio, *União Química Prevê Iniciar Produção da Sputnik V Nesta Semana*, https://ictq.com.br/industria-farmaceutica/2472-uniao-quimica-preve-iniciar-producao-da-sputnik-v-nesta-semana (last visited Dec. 6, 2022).

[21] Ricardo Brito & Polina Ivanova, *Brazil Health Regulator Rejects Russia's Sputnik vaccine*, Reuters (Apr. 26, 2021), www.reuters.com/world/americas/brazil-health-regulator-anvisas-technical-staff-recommend-against-importing-2021-04-26/ (last visited Feb. 14, 2023); Sofia Moutinho, *Brazil Gives Russian COVID-19 Vaccine a Chance, Approving the Import of Limited Doses*, Science, AAAS (Jun. 9, 2021), www.science.org/content/article/brazil-gives-russian-covid-19-vaccine-chance-approving-import-limited-doses (last visited Dec. 6, 2022).

[22] Leonardo Benassato, *União Química Finaliza Primeiro Lote de Vacina Russa Contra Covid-19 Sputnik V*, Reuters (May 20, 2021), www.reuters.com/article/saude-covid-lote-uniaoquimica-idLTAKCN2D129S (last visited Dec. 6, 2022).

[23] Sputnik-V relies on different adenoviruses for the two shots in the primary series, Ad26 for the first shot and Ad5 for the second. According to an informant at União Química, they produced the drug substance for both shots, but substantially more of the first than the second (indeed, the second shot for Sputnik-V was in short supply globally).

fill–finish of Sputnik-V by Probiomed,[24] and the following year it was reported that Probiomed may produce the drug substance too,[25] but it does not appear that the Russian vaccine was ever produced locally in Mexico. In Peru, the government announced in September 2021 that it would build a plant for fill–finish of Sputnik-V, though without providing details, and there is little evidence that the project advanced.[26]

A record of multiple announcements with less follow-through is a notable trait of the Russian vaccine during the pandemic. The announcements themselves led some observers to depict Sputnik as a vaccine with an expansive global manufacturing network and to laud the vaccine's sponsor for its willingness to engage in technology transfer.[27] Yet drug substance production for Sputnik vaccine remained highly centralized,[28] and not as much of the technology transfer for fill–finish that was being celebrated actually happened either.

A notable absence from the account of LAC production of viral vector vaccines is Johnson & Johnson.[29] As this is the same technology as AstraZeneca, CanSino, and Sputnik, requiring the same sorts of production capabilities and infrastructure, the challenges to technology transfer and manufacturing would not appear to be greater for J&J. The absence is particularly surprising – indeed, a missed opportunity – given J&J's large presence in the region, and therefore familiarity with local productive landscapes, regulatory processes, and procurement and distribution systems, all of which presumably would have eased the establishment of partnerships. In Brazil, officials from BioManguinhos had discussions with J&J, but opted to pursue AstraZeneca on account of that company's greater willingness to transfer technology for full production, as well as expectations that the vaccine would be ready to

[24] This arrangement also included Birmex, a state-owned laboratory linked to the Secretariat of Health that was in charge of Sputnik's local registration and distribution. Berenice Esquivel, *México se Aliará con Rusia Para Envasar y Producir Vacuna Sputnik V*, Sobre La Mesa MX (2021), https://sobrelamesamx.com/mexico-se-aliara-con-rusia-para-envasar-y-producir-vacuna-sputnik-v/ (last visited Dec. 8, 2022); Comunicación Social Birmex, *México envasará vacuna Sputnik V | Birmex*, https://birmex.gob.mx/2021/10/18/mexico-envasara-vacuna-sputnik-v/ (last visited Dec. 8, 2022).

[25] Minahil Waseem, *Mexican Lab Close to Launching Sputnik V Vaccine Production – Russian Ambassador*, Pakistan Point (Jul. 12, 2022), https://pakistanpoint.com/s/1535217 (last visited Feb. 15, 2023).

[26] Marcelo Rochabrun, *Peru to Build Plant to Make Sputnik V COVID-19 Vaccine – President*, Reuters (Sep. 7, 2021), www.reuters.com/world/americas/peru-build-plant-make-sputnik-v-covid-19-vaccine-president-2021-09-07/ (last visited Dec. 8, 2022).

[27] *Russia Pushes Ahead with Open License Approach to Sputnik V – Despite WHO Concerns over Manufacturing Practices*, Health Policy Watch (2021), https://healthpolicy-watch.news/russia-pushes-ahead-with-open-license-approach-to-sputnik-v-despite-who-concerns-over-manufacturing-practices/ (last visited Dec. 6, 2022); Amy Maxmen, *The Fight to Manufacture COVID Vaccines in Lower-Income Countries*, 597 Nature 455 (2021).

[28] According to Airfinity, roughly 95 percent of the drug substance output for this vaccine comes from Russia, with the small remainder from Belarus and Kazakhstan.

[29] Formally, this is Janssen, a pharmaceutical firm within the larger Johnson & Johnson health products conglomerate.

produce and use sooner.[30] Globally, in terms of the number of partners and geographic scope, J&J's global production approach has been limited: all of the drug substance production reported by Airfinity came from facilities in the Netherlands and the United States (the latter riddled with problems[31]); J&J partnered with producers in India and South Africa for fill–finish, but not in LAC.

B *Inactivated Virus*

The other vaccine type with production in LAC is the oldest and most traditional approach, based on inactivated viruses. During the pandemic, two vaccines from China were leaders in the production of vaccines of this sort: Sinovac (private) and Sinopharm (public). Together, these accounted for nearly 40 percent of all the COVID-19 vaccines produced globally. While these firms have established multiple agreements for partners throughout the world to engage in fill–finish, Airfinity reports that drug substance production remained entirely in China.

The most advanced manufacturing partnership in LAC for a vaccine of this type is between Sinovac and the Butantan Institute, a public research institute in São Paulo, Brazil.[32] According to this arrangement, Butantan, which was responsible for running Sinovac's Phase 3 clinical trial in Brazil, would commence with fill–finish based on imported drug substance, pending the trials being successful and the vaccine authorized for use in Brazil. Accordingly, Sinovac committed to technology transfer to facilitate local production.[33] The Sinovac/Butantan partnership also projected an eventual move upstream to drug substance, and thus full, integrated production. Butantan began constructing a new facility for this objective, but this stage of the partnership was not reached.

Information on additional production partnerships for inactivated virus vaccines remains scarce. Sinovac announced plans for technology transfer and local production in Chile, Colombia, and Ecuador. The Chilean project was reported as

[30] Elize Massard da Fonseca, Kenneth C. Shadlen & Helena de Moraes Achcar, *Vaccine Technology Transfer in a Global Health Crisis: Actors, Capabilities, and Institutions*, 52 Res. Policy 104739 (2023), at 4. União Química also reports discussions for technology transfer with J&J.

[31] *How Did 75M J&J Vaccines Get Ruined? FDA Details the Manufacturing Woes at Emergent's Beleaguered Site*, Fierce Pharma, www.fiercepharma.com/manufacturing/some-j-j-covid-19-doses-now-cleared-from-emergent-but-several-countries-are-already (last visited Dec. 6, 2022).

[32] Unlike BioManguinhos, which is linked to the Ministry of Health of the federal government in Brazil, Butantan is attached to the government of the state of São Paulo.

[33] *Doria Anuncia que Butantan Será Parceiro de Laboratório Chinês Para Vacina Contra o Coronavírus em Fase Final de Testes*, https://g1.globo.com/sp/sao-paulo/noticia/2020/06/11/governo-de-sp-diz-que-instituto-butantan-vai-produzir-vacina-contra-o-coronavirus.ghtml (last visited Dec. 6, 2022); Antonio Regalado, *Every Country Wants a Covid-19 Vaccine. Who Will Get It First?*, MIT Technology Review (Aug. 13, 2020), www.technologyreview.com/2020/08/13/1006314/take-your-best-shot/ (last visited Oct. 25, 2022).

including fill–finish facilities as well as an R&D center.[34] The Economic Commission for Latin America and the Caribbean (ECLAC) reported a Memorandum of Understanding between Sinovac and an unspecified partner in Colombia "for production, technology transfer and vaccine development projects, starting with fill and finish processes in the second quarter of 2022,"[35] while announcements of the agreement in Ecuador lack details on locations or technologies to be transferred.[36] With regard to Sinopharm, there is no record of production in Latin America, neither drug substance nor fill–finish. Discussions for production in Argentina were reported but appear not to have advanced.[37]

C *mRNA*

Both of the leading mRNA vaccines (BioNTech/Pfizer and Moderna) have relied on tight-knit production networks, using their own facilities or engaging small sets of contract manufacturers. Neither vaccine's initial production networks included partners in Latin America.[38] In the case of Pfizer, this began to change in late 2021 and early 2022, as an agreement was announced with Eurofarma in Brazil, whereby the Brazilian firm would import the drug substance and undertake the fill–finish steps.[39] Moderna, though announcing its intention to build a facility in Africa, has not given similar signals about production in LAC. Rather, in February

[34] Cecilia Yáñez & Daniela Silva y Claudia Soto, *Más de 60 Millones de Dosis: Sinovac Confirma llegada a Chile Con Construcción de Planta Para Fabricar Vacunas en la RM y un Centro de Investigación en Antofagasta*, La Tercera (Aug. 4, 2021), www.latercera.com/que-pasa/noticia/mas-de-60-millones-de-dosis-sinovac-anuncia-su-llegada-a-chile-con-construccion-de-planta-para-fabricar-vacunas-en-la-rm-y-un-centro-de-investigacion-y-desarrollo-en-antofagasta/3VJPCVNIUVCMXKIA3PPJT4BX5M/ (last visited Dec. 7, 2022).

[35] ECLAC, *supra* note 4, at 14.

[36] *Ecuador Confirma Acuerdo Para la Construcción de Una Planta de Sinovac*, Primicias, www.primicias.ec/noticias/sociedad/planta-vacunas-sinovac-ecuador-covid/ (last visited Dec. 6, 2022).

[37] In February 2022 an Argentinean delegation, including the President and the Governor of the Province of Buenos Aires, visited China at the start of the Winter Olympics, where announcements were made of "possibilities" of technology transfer and local production. *En su Primer día en China, el Presidente Participó de la Ceremonia Inaugural de los Juegos Olímpicos de Invierno Beijing* (2022), www.cancilleria.gob.ar/es/actualidad/noticias/en-su-primer-dia-en-china-el-presidente-participo-de-la-ceremonia-inaugural-de (last visited Dec. 6, 2022).

[38] Chad P. Bown & Thomas J. Bollyky, *How COVID-19 Vaccine Supply Chains Emerged in the Midst of a Pandemic*, 45 World Econ. 468 (2022); Maxmen, *supra* note 27; *Vaccine Manufacturing | Launch and Scale Speedometer*, https://launchandscalefaster.org/covid-19/vaccinemanufacturing (last visited Dec. 1, 2021).

[39] In 2021 Pfizer announced a similar agreement with Biovac, in South Africa. Ludwig Burger & Manas Mishra, *Brazil's Eurofarma to Make Pfizer COVID-19 Shots for Latin America*, Reuters (Aug. 26, 2021), www.reuters.com/world/americas/pfizer-biontech-sign-deal-with-brazils-eurofarma-make-covid-19-shots-2021-08-26/ (last visited Oct. 31, 2022); *South Africa's Biovac to Start Making Pfizer-BioNTech COVID-19 Vaccine in Early 2022 – Exec*, Reuters (Dec. 6, 2021), www.reuters.com/business/healthcare-pharmaceuticals/south-africas-biovac-start-making-pfizer-biontech-covid-19-vaccine-early-2022-2021-12-06/ (last visited Oct. 31, 2022).

2022 Moderna announced a commercialization and distribution arrangement for an Argentinean partner with affiliates throughout the region to import the finished vaccines and have responsibility for local logistics (such as registration, negotiations with purchasers, and delivery).[40]

D *Protein-Based*

The profile of technology transfer into the region for production of protein-based COVID-19 vaccines is blank. There is no record of agreements for manufacturing the Novavax product, which based all drug substance production in the United States and India. Nor are there confirmed plans for production of the Sanofi/GSK vaccine, an early front-runner that received public funding, and for which high demand in 2021 was projected and advance purchases were made.[41] The Texas Children's Hospital vaccine is not produced in the region either, despite the inventors' willingness to transfer technology widely.[42]

The absence of protein-based vaccines in the landscape of LAC production is curious, as the appropriate production capabilities are present. Indeed, much regional pre-pandemic vaccine production relied on this technological approach. During the pandemic, in addition to attempting to participate in production of vaccines via technology transfer, the focus of this chapter, several countries embarked on efforts to develop their own COVID-19 vaccines. Though not exclusively protein-based, most of the "home-grown" projects advanced in the region use this technological platform, further evidencing the existence of local capabilities for this sort of production.[43]

One instance of a protein-based COVID-19 vaccine produced in the region and authorized for use in a national vaccination program during the main period of the pandemic was from Cuba. Cuba did not participate in the COVAX program, nor

[40] *Moderna Signs Vaccine Distribution Service Agreement with Adium Pharma*, Pharmaceutical Technology (Feb. 23, 2022), www.pharmaceutical-technology.com/news/moderna-vaccine-agreement-adium/ (last visited Dec. 6, 2022).

[41] Sanofi has vaccine production facilities in the region, and Vargas reports that Sanofi indicated a plan to produce the vaccine in Mexico if trials were successful (Veronica Vargas, *Analysis of Regional Capacity for Research, Development, and Manufacturing of Vaccines in Latin America and the Caribbean*, Unpublished manuscript, Inter-American Development Bank (2020) at 28).

[42] Joe Palca, *Whatever Happened to the New No-Patent COVID Vaccine Touted as a Global Game Changer?*, NPR (Aug. 31, 2022), www.npr.org/sections/goatsandsoda/2022/08/31/1119947342/whatever-happened-to-the-new-no-patent-covid-vaccine-touted-as-a-global-game-cha (last visited Dec. 6, 2022); Peter J. Hotez & Maria Elena Bottazzi, *A Covid Vaccine for All*, Scientific American (Dec. 30, 2021), www.scientificamerican.com/article/a-covid-vaccine-for-all/ (last visited Feb. 20, 2023).

[43] The indigenous LAC vaccine projects are reviewed in ECLAC, *supra* note 4, at 69–73. See also Vargas, *supra* note 41. See also Martín De Ambrosio, *Covid-19: Latin America Defies Nationalism and Circumstance to Develop Its Own Vaccines*, 382 BMJ 1351 (2023).

did the government make purchases directly from foreign vaccine developers; its vaccination strategy relied wholly on developing and producing its own vaccines.[44] Cuba's vaccines have also been exported to a handful of countries within LAC (Nicaragua, Venezuela) and beyond (Iran, Vietnam), but for the most part they have been produced at limited scale for local use.

An important constraint on wider use of the Cuban vaccines has been production capacity on the island. Not only is manufacturing hindered by US sanctions, which complicate access to essential inputs, but the fact that three injections are needed to complete the primary course (plus more for boosters) obviously increases the amount of output needed.[45] In January 2022, the Central American Bank for Economic Integration announced plans to loan Cuba US$53.1 million to increase production capacity and, potentially, enable exports. The government of France is reported to have provided funds for manufacturing as well.[46] Cuba applied to the WHO for Emergency Use Authorization of the Soberana vaccines, which could have increased global demand and thus been important for attracting additional producers, though this process was not completed.[47] Although Cuban authorities have announced a willingness to transfer technology, and there are reports of technology transfer in Iran and Vietnam, it did not occur on a significant scale. This can be attributed in part to resource constraints in Cuba, in that the local experts with essential production knowledge are being allocated to production rather than outward technology transfer, as well as potential technology transfer recipients'

[44] Sara Reardon, *Cuba's Bet on Home-Grown COVID Vaccines Is Paying Off*, 600 NATURE 15 (2021); Luke Taylor, *Why Cuba Developed Its Own Covid Vaccine – and What Happened Next*, 374 BMJ n1912 (2021). In October 2023 another home-grown, protein-based vaccine was authorized in the region, in Argentina. *Argentine-Made Covid-19 Vaccine Approved*, MERCOPRESS (Oct. 19, 2023), https://en.mercopress.com/2023/10/19/argentine-made-covid-19-vaccine-approved (last visited Oct. 25, 2023).

[45] Abdala is a triple-dose vaccine. Soberana 2 consists of two doses, but it is combined with another vaccine, Soberana Plus, as part of a three-dose regimen. Protein-based vaccines are ordinarily formulated with adjuvants, to improve performance, though this does not appear to present a substantial constraint for the Cuban vaccines, which both use aluminum hydroxide.

[46] Mark Frank, *Central American Bank Funds Cuban COVID-19 Vaccine Drive*, NEWS.TRUST.ORG (Jan. 11, 2022), https://news.trust.org/item/20220111163115-gbvyo/ (last visited Dec. 6, 2022).

[47] Throughout the pandemic the WHO posted a regularly updated table of vaccines applying for authorization, *Status of COVID-19 Vaccines within WHO EUL/PQ Evaluation Process: Guidance Document*. Until well into 2023 the status reported by the WHO remained "Awaiting information on strategy and timelines for submission," and eventually (by Aug. 2023) the Cuban vaccines were removed from the document, suggesting that the process of obtaining WHO authorization had stopped. In October 2023, the WHO prequalification unit revamped its website, replacing its regularly updated table with a new document "COVID-19 Vaccines with WHO Emergency Use Listing," with no reference to the Cuban vaccines. *COVID-19 Vaccines with WHO Emergency Use Listing | WHO – Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)*, https://extranet.who.int/prequal/vaccines/covid-19-vaccines-who-emergency-use-listing (last visited Oct. 25, 2023).

lack of interest in producing vaccines that were not authorized by the WHO and thus not in high demand.

2 ASTRAZENECA IN LATIN AMERICA

Having provided an overview of the landscape of production partnership agreements in the region, I now examine in more detail the two most important cases: the technology transfer and manufacturing arrangements for production of the AstraZeneca vaccine in Brazil, and jointly in Argentina and Mexico. Both partnerships were supported by combinations of public and private financing to minimize the risks involved. To understand this important dimension of the COVID-19 response, we need to remember the urgency of the situation – not just the need for new vaccines, but large volumes of new vaccines that would be produced quickly. With a premium on speed, steps were taken to transfer technology and build production networks while the products were still in trials, so large-scale production could commence, and doses be available immediately upon (or soon after) receipt of marketing authorization. These expenditures were thus "at-risk," because if clinical trials revealed the vaccine candidates to be unsuccessful, the investments would be lost.[48]

A *Brazil*

The first partnership that AstraZeneca reached in the region was with BioManguinhos, announced in June 2020.[49] The AstraZeneca/BioManguinhos partnership stands out for its contribution to a national vaccination strategy. BioManguinhos was a principal supplier to the Brazilian Ministry of Health, particularly in 2021 when the pandemic was at the acute stage; at times AstraZeneca vaccines produced by BioManguinhos accounted for half of the vaccines used in Brazil.

The AstraZeneca/BioManguinhos partnership emerged from an intensive prospecting and evaluation exercise undertaken in Brazil. When the WHO declared COVID-19 a global pandemic in March 2020, a BioManguinhos team, working jointly with colleagues from the Ministry of Health, was already looking for vaccines that the institute could produce. From the start, technology transfer that would eventually allow for local production of the full vaccine was regarded as a key objective. Building upon – and expanding – an already-existing "prospecting"

[48] To be sure, pharmaceutical innovation always entails at-risk elements, as projects that fail in clinical trials and are not approved by regulators cannot be commercialized. What's distinct about the "at-risk" investments in the COVID-19 pandemic is that they were directed to so many downstream activities, to set up manufacturing facilities, and included substantial funding from governments and philanthropic organizations. Bhaven N. Sampat & Kenneth C. Shadlen, *The COVID-19 Innovation System*, 40 HEALTH AFF. (MILLWOOD) 400 (2021).

[49] This section draws on Fonseca, Shadlen & Achcar, *supra* note 30.

division, BioManguinhos set about evaluating candidates according to a range of criteria, including not just the state of development of the products and their appropriateness for Brazil's vaccination campaign, but also technological and manufacturing characteristics.[50]

BioManguinhos officials regarded the AstraZeneca vaccine, which emerged originally from the University of Oxford (United Kingdom), as particularly appropriate, as it was at an advanced stage of development, and the viral vector technology was complementary to its own existing competencies in working with cells in bioreactors. BioManguinhos thus expected that the manufacturing process would be fastest with the AstraZeneca vaccine, using its existing facilities and building on its capabilities in biologics. Fill–finish capacities used for Yellow Fever vaccines could be adjusted, for example, and cell culture for production of the drug substance could be accomplished in a plant with bioreactors that was equipped to produce interferon but would be redeployed. Also important was Oxford and AstraZeneca having announced their intent to build a global, distributed production network, which would feature transfer of technology to partners for manufacture of the full vaccine – not just fill–finish but drug substance too, and not just in Europe and the United States but also to partners in the Global South.[51]

The ensuing partnership was designed to proceed in two stages. First, BioManguinhos would import the drug substance, supplied by AstraZeneca, and complete the process of manufacturing the final drug product at its facilities in Rio de Janeiro, with an initial target of 30 million doses. Pending completion of clinical trials and regulatory approval of the vaccine, another 70 million doses would be produced under these arrangements. The completed doses would then be sold to Brazil's Ministry of Health, which had committed funds to purchase the 100 million doses. In the second stage, BioManguinhos would produce the drug substance too, and thus be manufacturing the full vaccine. While full production was the ultimate objective, the immediate priority was to be able to provide doses to the Ministry of Health, which, given the state of capabilities and infrastructure, would be accomplished most quickly via fill–finish.

[50] A Primeira Vacina 100% Brasileira Contra a Covid-19: A Conquista de Bio-Manguinhos/Fiocruz, 2–3 (Maurício Z. Medeiros et al. eds., 2022), https://portolivre.fiocruz.br/primeira-vacina-100-brasileira-contra-covid-19-conquista-de-bio-manguinhosfiocruz (last visited Feb. 14, 2023).

[51] Carina C. D. Joe et al., *Manufacturing a Chimpanzee Adenovirus-Vectored SARS-CoV-2 Vaccine to Meet Global Needs*, 119 Biotechnol. Bioeng. 48 (2022); Christopher Garrison, *How the "Oxford" Covid-19 Vaccine Became the "AstraZeneca" Covid-19 Vaccine*, Medicines Law & Policy (Oct. 5, 2020), https://medicineslawandpolicy.org/2020/10/how-the-oxford-covid-19-vaccine-became-the-astrazeneca-covid-19-vaccine/ (last visited Dec. 9, 2022); Tom Whipple, *The Vax Man*, The Times (Aug. 7, 2021), www.thetimes.co.uk/article/the-inside-story-of-the-oxford-astrazeneca-vaccine-meet-the-man-who-made-it-sk2k73j6v (last visited Sep. 1, 2021). Jorge L Contreras & Kenneth C Shadlen, *Contrasting Academic Approaches to COVID-19 Vaccine Production and Distribution: What Can the Oxford and Texas Experiences Teach Us about Pandemic Response?*, 2 Health Aff. Sch. qxae012 (2024).

While starting downstream with fill–finish operations and moving upstream to drug substance production is a common approach to technology transfer for vaccine production,[52] and one that previous BioManguinhos projects had followed as well, an important aspect of these arrangements in the case of the COVID-19 vaccine is that the steps were accelerated and collapsed. That is, preparation for the second stage started while the first was in process: BioManguinhos was procuring inputs, fitting the facilities for drug substance production, and getting its manufacturing plant and processes approved by the national health regulator (Anvisa), while also preparing for – and then engaging in – fill–finish production.

As an experienced vaccine manufacturer, BioManguinhos already had advanced capabilities in the core steps for fill–finish operations, including documentation, analytics, and quality control requirements, along with special-purpose "clean rooms." BioManguinhos worked with AstraZeneca to conform with the new standards that would be required and, importantly, to master the specific steps for this particular vaccine.[53] BioManguinhos raced to complete these steps and ready itself for undertaking the final steps in vaccine production. As one informant put it, "we should be waiting for the *IFA*, the *IFA* shouldn't be waiting for us."[54]

And, indeed, it was BioManguinhos that was made to wait, on account of problems within the AstraZeneca supply chain. Specifically, the drug substance that AstraZeneca was meant to supply (from a contract manufacturer in China) was delayed. Without the essential input, of course, BioManguinhos would be unable to proceed to production. Although the Ministry of Health managed to fill the gap by importing fully produced AstraZeneca vaccine doses (from the Serum Institute of India, another manufacturer in AstraZeneca's global production network), the experience demonstrates the vulnerability of fill–finish operations, specifically dependence on external suppliers. A benefit of developing upstream capabilities, to produce the drug substance too, as eventually occurred, is that it reduces vulnerability of this sort.

While both stages of the partnership involved the transfer of technology, know-how, and data, it was in the second stage that this was most critical. BioManguinhos had never produced a viral vector product before, and therefore had to learn to apply its existing capabilities and technology for cell culture in bioreactors and protein purification to the challenges of producing the drug substance for this type of vaccine, and, specifically, the AstraZeneca version.

[52] *Building a Successful Vaccine Manufacturing Business in Lower and Middle Income Countries: Lessons from Industry Leaders and Innovators*, UNIDO (2021), www.unido.org/sites/default/files/files/2022-01/3249%20-%20Unido%20Vaccine%20Manufacturing%20in%20LMICs%20document%20v4.pdf (last visited Dec. 21, 2022).

[53] Technology transfer for fill–finish involved transferring expertise in unfreezing the imported drug substance, formulation, and sterile injection of precise volumes into vials. All of this needed to be accomplished rapidly and with capacities to operate at high volumes, as part of pandemic response, and under strict quality control.

[54] "IFA" is Portuguese for active pharmaceutical ingredient (API), which is how the drug substance is referred to in Brazil.

A key stage of the collaboration involved receipt from AstraZeneca of the cell lines, virus seed, and culture medium. To achieve the same clinical results, BioManguinhos (and all the producers in AstraZeneca's global production network) would need to use the same starting materials and proceed following the same steps.[55] To prepare, BioManguinhos' staff received training to defrost biobanks, as the cell lines were shipped at –150°C. BioManguinhos received two capsules to train with. Just as BioManguinhos readied its equipment and processes to be "waiting for the IFA" in the first stage, it made sure to be prepared for receipt of the key starting materials from AstraZeneca for the second stage.

In June 2021, after the contract for the second stage of the technology transfer was signed, BioManguinhos received the cell lines and, continuing to work with AstraZeneca, initiated operations to produce the drug substance. In January 2022, BioManguinhos received regulatory approval of the drug substance, and the first batch of fully produced vaccine was delivered to the Ministry of Health in February 2022.

Before turning to the case of the other partnership for production of the AstraZeneca vaccine in the region, in Argentina and Mexico, three additional aspects of the AstraZeneca/BioManguinhos partnership are worth noting: the role of external support, the government's contributions, and the formal nature of the relationship between the parties. The AstraZeneca/BioManguinhos partnership benefitted from philanthropic and public support, both to set it up and to make it work. The Lemann Foundation sponsored AstraZeneca's clinical trials in Brazil, for example, and a consortium led by Brazil's largest bank (Itaú) and brewing company (Ambev) provided financing to help BioManguinhos adapt its manufacturing facilities, as well as aiding with logistics to help BioManguinhos manage the procurement of equipment and inputs.

The Brazilian government also provided support for technology transfer. This was both direct, through the allocation of resources, and indirect, via the exercise of a special procurement contract that allowed BioManguinhos to dedicate public resources toward developing a product that required regulatory approval at a point when such approval was outstanding. The national government's backing appears paradoxical, given the overall posture toward the pandemic and vaccines demonstrated by President Bolsonaro, who consistently downplayed the public health threats posed by the coronavirus, appears to have gone out of his way to demonstrate his rejection of WHO guidelines on nonpharmaceutical interventions such as masking and social distancing, and regularly made comments that discredited the value of vaccines and vaccination. Yet, notwithstanding these attributes and actions of the President, the federal government allocated resources and moved the machinery of government and bureaucracy to enable and advance BioManguinhos' partnership with AstraZeneca.[56]

[55] Joe et al., *supra* note 51.

[56] For more discussion of Bolsonaro's behavior and the politics of vaccination in Brazil, see Elize Massard Da Fonseca et al., *Presidential Denialism and the Subnational Government's Response*, *in* Coronavirus Politics: The Comparative Politics and Policy of COVID-19 (Scott L. Greer et al. eds., 2021); Elize Massard da Fonseca, Kenneth C. Shadlen &

With regard to its relationship with AstraZeneca, BioManguinhos was a licensee, not a contract manufacturer. Concretely, this meant that BioManguinhos was not producing for AstraZeneca, and the Ministry of Health was not purchasing the vaccine from AstraZeneca, but rather BioManguinhos was producing the vaccine and selling it directly to the government, with payment of a royalty (undisclosed amount) to AstraZeneca. Although the differences in this sort of relationship are not to be exaggerated, as what BioManguinhos could do with its output was restricted by the terms of the license set by AstraZeneca (and, as discussed, in the first stage the amount BioManguinhos could produce was constrained by how much drug substance AstraZeneca supplied), this distinction nevertheless marks an important difference with the other AstraZeneca partnership in the region.

B *Argentina–Mexico*

In contrast to the agreement with BioManguinhos in Brazil, where all production was to be done by the same producer in the same country, the second AstraZeneca partnership in Latin America, announced in August 2020, featured production in Argentina and Mexico. And while production in Brazil began with fill–finish steps, the Argentina–Mexico collaboration started immediately with both drug substance and fill–finish production. According to these arrangements, mAbxience, an Argentinean firm dedicated to producing "biosimilar" monoclonal antibodies, would manufacture the drug substance and ship it, frozen, to Mexico, for Liomont, one of Mexico's largest pharmaceutical companies, to undertake the fill–finish stages. Then, the final products would be distributed by AstraZeneca throughout the LAC region (except Brazil). This partnership involved philanthropic support too, with the Mexico-based Carlos Slim Foundation providing direct financing and interest-free loans to both partners.[57]

An immediate question that emerges here is why not have both steps, drug substance and fill–finish, in Argentina or in Mexico. That is, why not emulate the arrangement that AstraZeneca had established in Brazil (and elsewhere, though not everywhere[58]), with technology transfer for drug substance and fill–finish in the

Francisco I. Bastos, *The Politics of COVID-19 Vaccination in Middle-Income Countries: Lessons from Brazil*, 281 Soc. Sci. Med. 1982 114093 (2021).

[57] López Obrador Promete que la Vacuna Contra el Coronavirus Será Gratuita y Universal, La Nacion (Aug. 13, 2020), www.lanacion.com.ar/el-mundo/el-gobierno-mexicano-promete-vacuna-coronavirus-sera-nid2420439/ (last visited Dec. 11, 2022); *La Argentina Fabricará una Vacuna Contra el Coronavirus y Estará Disponible en el Primer Semestre de 2021*, Clarín (Aug. 12, 2020), www.clarin.com/politica/alberto-fernandez-anuncia-argentina-fabricara-vacuna-coronavirus_0_GWSf6lVKU.html (last visited Dec. 7, 2022).

[58] It's not uncommon for drug substance and fill–finish operations to be separated geographically. AstraZeneca's supply chain for the EU featured drug substance production in the Netherlands and fill–finish in Spain, for example, and the supply chain for the United States involved producers in different states. Bown & Bollyky, *supra* note 38.

same country? Although locating both stages in Argentina seems feasible, given the presence of multiple firms with experience producing biosimilars and sterile injectables that could have been enlisted for fill–finish, it appears that AstraZeneca sought a geographically distributed supply chain for Latin America, rather than concentrate all production in South America – and in the southern reaches of the continent.

In fact, had AstraZeneca found a partner in Mexico, it is not clear that Argentina would have been involved at all. According to actors involved, the origins of the partnership featured AstraZeneca approaching the Slim Foundation as a potential funder of at-risk investment needed for its "no profit, no loss" model, which then identified Liomont. The Mexican firm, unable to satisfy AstraZeneca's needs on its own, and having a long-standing relationship with another firm that was part of Grupo Insud, the conglomerate that included mAbxience, brought the Argentinean lab into the partnership. According to this version, AstraZeneca did not immediately seek a partner in Argentina, but rather found mAbxience via Liomont.[59]

The AstraZeneca partnership with mAbxience and Liomont did not meet expectations in terms of output. Drug substance production occurred quickly, on account of mAbxience's existing capabilities (human and physical) and its abilities to recondition its facilities to absorb the technology from AstraZeneca, but fill–finish operations in Mexico did not advance at the expected pace. Projected to produce 150–250 million doses, the collaboration did not reach that target; as of the end of 2021, only 70 million final doses of the jointly produced vaccine had been delivered throughout the LAC region.[60]

The sources of the delays in the final production of doses are different in this case than at BioManguinhos. In Brazil, the delays were due to the unavailability of the drug substance needed to take the final steps. In the case of the Argentina–Mexico collaboration, Liomont received drug substance from mAbxience in January 2021, but experienced difficulties undertaking the steps that it was contracted for, which led to frozen drug substance needing to be stored in warehouses.[61] One reason for this was that Liomont faced delays in obtaining certification of its new facility for vaccine production, but even when the plant had the green light it was hamstrung by a lack of access to filters, pumps, and other production inputs on account of

[59] Note that ECLAC refers to a technology transfer agreement between AstraZeneca and the Slim Foundation, not between AstraZeneca and the companies themselves. ECLAC, *supra* note 4, at 14.

[60] Elías Camhaji & Federico Rivas Molina, *El Largo y Complejo Viaje de los 250 Millones de "Vacunas Latinoamericanas" de AstraZeneca*, El País (Dec. 3, 2021), https://elpais.com/internacional/2021-12-03/el-largo-y-complejo-viaje-de-los-250-millones-de-vacunas-latinoamericanas-de-astrazeneca.html (last visited Dec. 7, 2022). According to a post in June 2022 on LinkedIn by the director of Mexico's drug regulator, roughly 90 million doses had been distributed to LAC countries. Alejandro Svarch, Linkedin (2022), www.linkedin.com/posts/alejandrosvarch_covid-activity-6937197640824619008-Y6HH (last visited Dec. 7, 2022).

[61] Though the problems encumbering final production differed, both illustrate the difficulties of building and maintaining global supply chains in the context of a pandemic.

strained supply chains. Compounding these challenges, the use of the Defense Production Act in the United States required all US-based producers of inputs to prioritize orders placed by firms manufacturing COVID-19 countermeasures for the US government, creating difficulties for manufacturers outside the United States (like Liomont) to obtain essential inputs from US suppliers. Unable to obtain the equipment needed, Liomont initially was unable to apply the finishing stages to the drug substance produced by mAbxience according to the programmed schedule.[62] By late May 2021 the bottlenecks at Liomont were finally overcome, and from that point production as envisioned in the agreement from the previous year was realized.

The delays in production opened the agreement to intense criticism. To be sure, the delays were not massive: when the agreement was announced in August 2020 it was projected that, pending positive clinical trial results, doses would be distributed beginning in April 2021;[63] and doses started arriving by the end of May. Yet context is critically important: the vaccines were missing when they were most needed. The first half of 2021, precisely the period when finished doses based on drug substance produced by mAbxience were not yet – or only just beginning to – be distributed, marked the peak of the pandemic in Latin America and the Caribbean, when excess death rates were accelerating (see Figure 15.1). While vaccination was advancing rapidly in the United States and Europe, much of the rest of the world still experienced low vaccination rates due to limited access to doses.[64] In this context, an otherwise small delay of 6–8 weeks had enormous consequences.

Not surprisingly, criticisms of the agreement were most intense in Argentina, where mAbxience was producing the drug substance, to great fanfare, but doses were unavailable for the local population. The secure supply of vaccines that production was promised to yield when the partnership was announced had not materialized, a source of great frustration – particularly given the country's own pharmaceutical production capabilities. Analyzing the criticisms that these delays elicited, and the subsequent debate over possible responses, provides important insights into the challenges of technology transfer.

[62] Liomont was not unique in being negatively affected by the Defense Production Act. According to an expert report commissioned by the National Academies of Sciences (US), "Vaccine manufacturers in other countries [outside the US] expressed concerns regarding their ability to obtain critical inputs either directly from the United States or in competition with the United States in the marketplace." National Academy of Medicine, *supra* note 9, at 63.

[63] *Los Interrogantes aún Pendientes Sobre la Vacuna que Espera la Argentina*, La Nacion (Sep. 13, 2020), www.lanacion.com.ar/politica/los-interrogantes-aun-pendientes-sobre-la-vacuna-que-espera-la-argentina-nid2448527/ (last visited Dec. 6, 2022).

[64] The situation was worsened by the spread of the Delta variant in 2021. Its devastating effect in India led to exports of the AstraZeneca vaccine produced by the Serum Institute being prohibited. *India Blocks Vaccine Exports in Blow to Dozens of Nations*, Financial Times (Mar. 25, 2021).

One criticism regarded the logic of the arrangements themselves, with drug substance produced in Argentina being shipped to Mexico for fill–finish, only for the final doses then to be shipped back to Argentina (and throughout LAC, other than Brazil). Some regarded this as unnecessary, as other Argentinean firms had capabilities to execute the fill–finish stage of production. Indeed, two of these firms (Sinergium and Biogénesis Bagó) are neighbors of the mAbxience plant where the drug production was occurring, located in the same industrial park (and also part of Grupo Insud). And if not these specific companies, other laboratories that make biosimilars or sterile injectables presumably could have been engaged early in the process to absorb the technology from AstraZeneca and perform the fill–finish steps locally. Considering the abundant production capabilities in Argentina's pharmaceutical sector, this appeared to be a missed opportunity, a shortcoming in the original design of the arrangements made in August 2020.

In addition to criticisms of the technology transfer and production partnership as it was originally designed, in 2021, with the supply crisis apparent, there were also calls for the Argentinean government to intervene to alter the arrangements in course. Protesters assembled outside the mAbxience factory, demanding that the plant's output not be shipped to Mexico but rather sent to another laboratory in Argentina for completion.[65] Protests making the same demand occurred outside the Ministry of Health offices in the capital.

Were the Argentine government to have introduced measures that overwrote an existing contract to enhance local supply of the vaccine, it would not have been unprecedented in the COVID-19 pandemic. As noted, the United States used the Defense Production Act to limit the export of inputs, notwithstanding contractual agreements that US manufacturers had with foreign producers, and India imposed an export ban that overrode the terms of the Serum Institute's contract with AstraZeneca. Argentina had already restricted exports of key inputs early in the pandemic (March 2020), mostly personal protective equipment, but also the medicine interferon.[66] Hypothetically, the Argentinean government could have stepped in, on an emergency basis, and demanded that some mAbxience-produced drug substance, which legally belonged to AstraZeneca and was meant to be sent to Mexico, be kept in the country; that the fill–finish be undertaken by another Argentinean lab; and that the completed doses be used locally in the national

[65] *Protestaron en el Laboratorio Mabxience que Fabrica las Vacunas en Argentina*, Zona Norte Hoy (May 6, 2021), www.zonanortehoy.com/escobar/sociedad/2021/5/6/protestaron-en-el-laboratorio-mabxience-que-fabrica-las-vacunas-en-argentina-94577.html (last visited Dec. 6, 2022); *Grupo Argentino de Izquierda Protesta Frente a Fabricante de Vacuna COVID-19 en Medio de Retrasos*, Reuters (Mar. 29, 2021), www.reuters.com/article/salud-coronavirus-vacunas-argentina-idltakbn2bl324 (last visited Dec. 6, 2022).

[66] Decree No. 317/2020, Mar. 28, 2020, B.O. (Arg.). *The World Trade Organization Provides a List of Export Restrictions Taken during the Pandemic: WTO | COVID-19: Measures Affecting Trade in Goods* (Oct. 20, 2022), www.wto.org/english/tratop_e/covid19_e/trade_related_goods_measure_e.htm (last visited Dec. 6, 2022).

vaccination campaign. Though such violations of the contract with an international firm could have had legal and geopolitical repercussions, it was regarded by some as justified given the urgency of the situation.[67]

Even had these steps been attempted, however, they almost certainly would not have had the desired effect of increasing output and thus the supply of vaccines available to the government. Understanding why is essential for getting to the heart of the challenges of vaccine production in the context of a global pandemic.

The most important obstacles that would have confounded any plans to sequester drug substance to complete doses locally are found in the areas of technology transfer and pharmaceutical regulation. For such plans to succeed, there would need to be technology transfer from AstraZeneca to the local fill–finish partner enlisted to take on this task, be it Sinergium, Biogénesis, or another firm.[68] As this was not part of the original arrangements, there were no firms ready to receive mAbxience's output and start fill–finish operations; getting one up to speed would take months. In this regard, references to the Indian government's restrictions of exports ("they did it, so why can't we?") are misleading, as, at the time of that government's intervention, the Serum Institute had already mastered fully integrated manufacturing of the vaccine.

Furthermore, unless AstraZeneca also amended its regulatory submissions to include a new Argentinean manufacturer, the version of the vaccine being produced (hypothetically) entirely within Argentina would need to undergo its own clinical trials, a lengthy process that would defeat the purpose of the emergency intervention. The mAbxience/Liomont version had been authorized by the WHO, with AstraZeneca as the license holder (the other labs involved were contract manufacturers, working on behalf of AstraZeneca), indicating that drug substance was produced in Argentina and fill–finish executed in Mexico. Revising regulatory submissions entails more than simply adding a new manufacturer to the list of producers. AstraZeneca would have to work with the local producer to achieve the desired output and the necessary standards – that is, to replicate the outcome produced by its collaboration with Liomont, and AstraZeneca would need to supply documentation to regulators that the new plant's production processes (including records and quality control) satisfied the required levels. Even if, hypothetically, AstraZeneca were prepared to do all of this, these steps would take time, again defeating the purpose of an emergency intervention to increase supply during the pandemic.

[67] One Argentine commentator drew a comparison with the UK government's commandeering of private cruise liners during the 1982 Argentina–UK war in the South Atlantic. Daniel E. Arias, *Abran Paso a una Vacuna Argentina – 1° Parte*, AGENDAR (Sep. 29, 2021), https://agendarweb.com.ar/2021/09/29/abran-paso-a-una-vacuna-argentina-1-parte/ (last visited Oct. 25, 2022).

[68] Even this scenario implies that there was a firm that had the interest and available capacity to participate in such a scheme.

Argentina's health authorities were aware of these constraints. The Ministry of Health expressed concerns about the lack of supply, both to the UK's Ambassador to Argentina and to AstraZeneca officials, regarding this as nonfulfillment of the contract.[69] Yet there was little they could do with regard to manufacturing; the drug substance produced by mAbxience belonged to AstraZeneca, and setting up local fill–finish of this material – even with AstraZeneca's support – would not be possible within a realistic time frame. To be sure, some articles in the Argentinean press report that the government requested AstraZeneca to allow fill–finish to be done locally and threatened to impound drug substance produced by mAbxience for this end (usually one article repeating what another article reported), but informants in the Ministry of Health deny this, emphasizing that they knew it was not feasible. The Ministry was urging AstraZeneca to treat the supply crisis with urgency and take all necessary steps to fulfill its commitments to deliver the number of doses that Argentina had purchased.[70]

AstraZeneca's response did involve introducing a new supplier for the LAC supply chain and revising its regulatory dossier, but without embarking on fill–finish operations in Argentina. To overcome the bottleneck created by Liomont's delayed production, AstraZeneca redirected some of the drug substance produced by mAbxience to a contract manufacturer in the United States, Albany Molecular Research Inc (AMRI), a firm that had originally been engaged to undertake the fill–finish step for the US supply chain.[71] Thus the initial doses of the AstraZeneca vaccine that were distributed in the LAC region (outside of Brazil) were Argentina–United States rather than Argentina–Mexico products.

[69] The supply problem was not just due to production challenges in Mexico, but evidently how AstraZeneca went about allocating doses throughout the region.

[70] Eduardo Menegazzi, *Vizzotti y Nicolini Buscarán en Cambridge Avanzar en un Acuerdo con AstraZeneca Para Fabricar Completamente la Vacuna en Argentina*, Infobae (Jul. 14, 2021), www.infobae.com/politica/2021/07/14/vizzotti-y-nicolini-buscaran-en-cambridge-avanzar-en-un-acuerdo-con-astrazeneca-para-fabricar-completamente-la-vacuna-en-argentina/ (last visited Oct. 25, 2022); *¿Y las Vacunas que se Iban a Envasar en México? Argentina Enfurece Contra AstraZeneca*, El Financiero (May 3, 2021), www.elfinanciero.com.mx/mundo/2021/05/03/y-las-vacunas-que-se-iban-a-envasar-en-mexico-argentina-enfurece-contra-astrazeneca/ (last visited Dec. 11, 2022); *Liberen las Patentes. La Izquierda Tenía Razón: Ahora Vizzotti Propone Envasar en Argentina la Vacuna de AstraZeneca*, La Izquierda Diario – Red internacional (May 3, 2021), www.laizquierdadiario.com/La-izquierda-tenia-razon-ahora-Vizzotti-propone-envasar-en-Argentina-la-vacuna-de-AstraZeneca (last visited Dec. 6, 2022).

[71] Kyle Blankenship, *AstraZeneca Signs on Albany Molecular to Help Boost COVID-19 Shot Production*, Fierce Pharma (2020), www.fiercepharma.com/manufacturing/astrazeneca-signs-albany-molecular-to-help-boost-covid-19-shot-production (last visited Dec. 11, 2022); *Vacuna del Covid: por qué las Dosis de AstraZeneca Todavía Llegarán de EE.UU. Y no de México*, Clarín (Jun. 11, 2021), www.clarin.com/sociedad/vacuna-covid-dosis-astrazeneca-todavia-llegaran-ee-uu-mexico_0_NVzdpow3m.html (last visited Dec. 6, 2022); Frank Jack Daniel, *Millions of AstraZeneca Doses Head to Mexico under Latin America Plan*, Reuters (May 21, 2021), www.reuters.com/world/americas/argentina-sending-mexico-material-4-mln-astrazeneca-doses-2021-05-21/ (last visited Dec. 11, 2022).

To understand the feasibility of this shift in light of the obstacles discussed in the previous paragraphs, it is important to note that, although AstraZeneca never obtained authorization of its COVID-19 vaccine in the United States, it had originally intended to do so, and to that end had established a US-based supply chain, with the necessary technology transfer undertaken and a set of producers indicated to the Food and Drug Administration (FDA). Thus, engaging AMRI, which already had been trained to produce the AstraZeneca vaccine, did not require additional technology transfer, as would have been the case with a new producer in Argentina. Nor did AMRI need to obtain new equipment to produce, as a new Argentinean firm would have.[72] And because the AstraZeneca vaccine was not being used in the United States, and therefore there was no domestic demand for the final product, AMRI's exports were not constrained by the Defense Production Act. Lastly, as regards regulation, because the US firm was already an FDA-approved producer (even if AstraZeneca's vaccine never had the FDA's authorization for use in the United States), the required changes to regulatory dossiers were more straightforward.

Before concluding, it is worth considering another potential producer to undertake the fill–finish steps of the drug substance produced by mAbxience: BioManguinhos. Like AMRI, BioManguinhos had already received technology transfer, so some of the obstacles discussed earlier would have been less present. At one point this was contemplated too, though several factors mitigated against this approach being explored. First, BioManguinhos did not have available capacity to simultaneously produce vaccines for Brazil, as it needed to do, and also undertake fill–finish steps to produce vaccines for the rest of the LAC region. Unlike in the case of AMRI and the United States, where fill–finish capacities were available without any demand for the final product, the AstraZeneca vaccine was authorized in Brazil and constituted a major part of the country's COVID-19 vaccination strategy. Second, BioManguinhos' authorization was by Anvisa, and, notwithstanding the recognition of the Brazilian regulator's attributes,[73] altering the regulatory dossier to include a firm authorized by Anvisa would be a more complicated process than making an alteration to include a firm designated as an authorized producer by the FDA.

3 TECHNOLOGY TRANSFER AND PRODUCTION OF COVID-19 VACCINES: COLLABORATION V. COMPETITION

None of the arrangements reviewed in this chapter featuring technology transfer for local production constitute independent manufacturing undertaken by LAC firms. That includes the AstraZeneca arrangements discussed in the previous section, the

[72] Indeed, it is likely that, were a new Argentinean partner enlisted for fill–finish, this firm would have encountered the same difficulties as Liomont experienced.

[73] PAHO, Regulatory System Strengthening in the Americas. Lessons Learned from the National Regulatory Authorities of Regional Reference (2021).

most advanced examples of local vaccine production in Latin America. In the case of mAbxience and Liomont, these firms were contracted by AstraZeneca to produce for a regional supply chain; mAbxience had no rights to or control over the drug substance it produced, and the same is so for the final doses produced by Liomont – all of this belonged to AstraZeneca.[74] Nor would it be accurate to describe BioManguinhos as independent, despite being a licensee rather than contract manufacturer. Even in the second stage of the partnership, when making the full vaccine itself and thus no longer dependent on AstraZeneca for the supply of drug substance, what BioManguinhos could do with its output remained limited by the conditions imposed by AstraZeneca.[75] These arrangements were partnerships for production of originator products via technology transfer; they did not feature local firms involved in the independent manufacturing of their own "generic" versions of these products.

While these characteristics of the vaccine production arrangements may be regarded as limitations, in that the local actors were not making independent and autonomous decisions about production and distribution,[76] they also came with advantages: local labs benefitted from technology transfer, and the vaccines they produced were not required to go through their own clinical trials but rather were included in the originators' dossiers and authorization processes. In normal times, such advantages might be outweighed by the disadvantages of lacking control and being in a subordinate position to the originator firms, but in the midst of a global pandemic the calculus may differ. That is, when massive amounts of output are needed as quickly as possible, it is not clear that independent production is the most fruitful path. For all of the difficulties that the joint Argentina–Mexico scheme for production of the AstraZeneca vaccine faced, for example, proceeding without the originator would have been even slower and less fruitful.

These characteristics of production during the pandemic have important implications for debates over intellectual property (IP) rights.[77] Where production

[74] Indeed, that is why the scenarios proposed in the previous section were unrealistic without AstraZeneca's engagement.

[75] Jamil Chade, *Acordo revela que AstraZeneca impôs restrições ao Brasil na vacina da covid*, UOL Notícias (Oct. 8, 2020), https://noticias.uol.com.br/colunas/jamil-chade/2020/10/08/acordo-de-base-revela-que-astrazeneca-impos-restricoes-ao-brasil-na-vacina.htm (last visited Feb. 16, 2023).

[76] Daniel Blinder, Lautaro Zubeldía & Sofya Surtayeva, *Covid-19 and Semi-Periphery: Argentina and the Global Vaccines Research and Development*, 27 J. World-Syst. Res. 494 (2021).

[77] Tahir Amin & Aaron S. Kesselheim, *A Global Intellectual Property Waiver Is Still Needed to Address the Inequities of COVID-19 and Future Pandemic Preparedness*, 59 Inq. J. Health Care Organ. Provis. Financ. 00469580221124821 (2022); Siva Thambisetty et al., *The TRIPS Intellectual Property Waiver Proposal: Creating the Right Incentives in Patent Law and Politics to end the COVID-19 Pandemic* (2021), https://papers.ssrn.com/abstract=3851737 (last visited Feb. 16, 2023); Julia Barnes-Weise, Ana Santos Rutschman & Reid Adler, *Assessment of the Proposed Intellectual Property Waiver as a Mechanism to Address the COVID-19 Vaccine Scarcity Problem*, 76 J Epidemiol Community Health 317 (2022); Bryan Mercurio, *The IP Waiver for COVID-19: Bad Policy, Bad Precedent*, 52 IIC – Int. Rev. Intellect. Prop. Compet. Law 983 (2021); Maxmen, *supra* note 27.

depends on the active engagement of originators, to help master production processes and satisfy regulatory requirements as quickly as possible, as is essential for vaccines during a pandemic, the absence or removal of IP rights is unlikely to increase supply quickly. What is needed in such circumstances is not subtractive – that is, removing the restrictions that IP rights create – but rather additive – that is, technology transfer from the originator to partners. In contrast, then, to what was witnessed with HIV/AIDS medicines earlier in the century, where the absence of patents and the existence of simple regulatory pathways enabled generic producers (public and private) to make abundant and affordable treatments available,[78] efforts to expand global supply of vaccines during the COVID-19 pandemic needed to rely on originator firms transferring technology, know-how, and data to manufacturing partners. Where such sharing does not happen, independent production of vaccines may still occur, but is likely to proceed at a substantially slower pace, which places severe limits on its usefulness during a pandemic.[79]

Importantly, the LAC partners involved in the production of vaccines did not regard the forms of collaboration as being restrictive, but rather as creating opportunities that could generate new capabilities. The fact that BioManguinhos was working under the conditions set by AstraZeneca according to the terms of the licensee was not regarded as a drawback. To the contrary, BioManguinhos officials knew that on their own they could not produce the vaccine fast enough. In fact, BioManguinhos officials expressed excitement regarding capability enhancement that the collaboration would bring. Accessing the adenovirus, viral vector technology, it was expected, would position BioManguinhos on a new research and knowledge pathway. Although its immediate objective was to contribute to the COVID-19 pandemic response in Brazil by manufacturing vaccines, the technology transfer promised by this partnership would grant BioManguinhos access to a new technological platform that could be applied to additional products going forward. Working closely with AstraZeneca not only enabled a faster route to COVID-19 vaccine production in Brazil, but, BioManguinhos officials stress, the acquisition of new competencies in a new technological area generates possibilities for collaboration with more external actors.[80]

[78] Brenda Waning, Ellen Diedrichsen & Suerie Moon, *A Lifeline to Treatment: The Role of Indian Generic Manufacturers in Supplying Antiretroviral Medicines to Developing Countries*, 13 J. Int. AIDS Soc. 35 (2010); Maurice Cassier & Marilena Corrêa, *Patents, Innovation and Public Health: Brazilian Public-Sector Laboratories' Experience in Copying AIDS Drugs*, in Economics of AIDS and Access to HIV-AIDS Care in Developing Countries: Issues and Challenges (Jean-Paul Moatti et al. eds., 2003).

[79] To illustrate, witness the efforts of the WHO's mRNA hub, launched in 2021 to produce an independent version of the Moderna vaccine which proceeded without Moderna's cooperation and engagement. According to the WHO, the first approval for human use "could potentially be in 2024." *FAQ – The mRNA Vaccine Technology Transfer Hub*, www.who.int/initiatives/the-mrna-vaccine-technology-transfer-hub/faq (last visited Feb. 16, 2023).

[80] Fonseca, Shadlen & Achcar, *supra* note 30; Maurício Z. Medeiros et al., *Vaccine Innovation Model: A Technology Transfer Perspective in Pandemic Contexts*, 40 Vaccine 4748 (2022).

Similarly in Argentina, the collaboration with AstraZeneca was seized by mAbxience as an opportunity. Although already an accomplished firm with proficiency in biological processes, and always regarding the shift to vaccine production as a temporary deviation from its core activities, mAbxience officials expected to benefit from the transfer of skills regarding business operations (for example, product, audits, purchasing, record-keeping).[81] Working with AstraZeneca to obtain approval of the vaccine from the European Medicines Agency, for example, required the introduction of new practices regarding data collection and documentation, changes that would be useful for placing its own products in the EU market. Moreover, mAbxience officials regarded this as the potential start of a new relationship as a local partner for one of the world's largest pharmaceutical firms with a portfolio (and pipeline) of innovative products. While BioManguinhos officials referred to the acquisition of capabilities that will allow it to take on new projects, mAbxience officials stressed the new commercial opportunities that arise from working with a firm such as AstraZeneca.[82] Officials of Liomont, in Mexico, expressed similar sentiments. And, though neither the União Química nor Richmond collaborations for the production of Sputnik-V advanced far, representatives from both of those firms explicitly regarded their relationships as opportunities.[83]

In fact, none of the actors involved in local vaccine production that I spoke with for this project expressed concern about their activities being constrained by originator firms' exercise of IP rights. Nor did they cite IP rights as a barrier to entry. Given my own priors, based on research of conflicts between Latin American and transnational pharmaceutical firms over IP rights,[84] this was surprising. Yet local firms repeatedly explained that originators' IP rights were not getting in the way of their abilities to produce COVID-19 vaccines in the pandemic, emphasizing, to the contrary, that even in the absence of any IP rights they would not have been producing COVID-19 vaccines on their own.[85]

[81] This can be regarded as a type of "buyer-driven upgrading," where a local firm experiences improvement in its production processes as a result of its role as supplier to an international lead firm (Eric Verhoogen, *Firm-Level Upgrading in Developing Countries*, 61 J. Econ. Lit. 1410 (2023)). In the present case, focus is on the active engagement between the originator and the local firm through technology transfer and the sharing of know-how and data.

[82] In 2022 mAbxience was acquired by the German firm Fresenius Kabi. *Fresenius Kabi Takes Control of mAbxience to Bolster Biosimilars*, Generics Bulletin (Mar. 31, 2022), https://generics.pharmaintelligence.informa.com/GB151774/Fresenius-Kabi-Takes-Control-Of-mAbxience-To-Bolster-Biosimilars (last visited Dec. 7, 2022).

[83] Even the local distributor of Moderna, an Argentinean firm for which manufacturing remains only a possibility that may eventually be realized eventually, embraces the relationship as a new commercial opportunity.

[84] Kenneth C. Shadlen, Coalitions and Compliance: The Political Economy of Pharmaceutical Patents in Latin America (2017).

[85] In the case of the AstraZeneca vaccine, which experienced the most advanced production in the LAC region, patent protection appears minimal in the countries where it was being produced. Although scientists from Oxford University, the original inventors who licensed the product to AstraZeneca for global production and distribution, had obtained patents on the

These observations have broader implications for how we think about technology transfer and local production. In contrast to the prominent image of renegade pharmaceutical producers in the Global South, an image forged by the experience of the HIV/AIDS crisis that featured Indian firms launching their own products and thereby challenging the power and influence of the international pharmaceutical industry, the firms involved in local production of COVID-19 vaccines in Latin America were working closely with the originators. And they were content to be doing so; partnerships were appreciated as being beneficial more than resented as being constraining. To be sure, there are certainly rebellious firms in the region that may have wished to confront "big pharma," as they still do with many medicines, but without the engagement of the originators they had little chance of producing COVID-19 vaccines during the pandemic.

4 DISCUSSION AND CONCLUSION

Technology transfer for production of COVID-19 vaccines in Latin America and the Caribbean was less extensive than might be expected from a region with many middle-income countries that have important pharmaceutical sectors.[86] Most activities observed during the pandemic consisted of LAC firms applying the final steps to prepare vaccines, using drug substance imported from outside the region. Outside of Cuba, which developed and produced its own vaccines, only two LAC manufacturers, Brazil's BioManguinhos and Argentina's mAbxience, advanced significantly on manufacturing drug substance; and only BioManguinhos produced the full vaccine – that is, drug substance plus fill–finish.

This final section explores some of the factors accounting for this scenario and explores the obvious question of whether there could have been more. Focus is directed at three sets of issues: the interest of vaccine developers to partner with local manufacturers; the extent of vaccine production capabilities in the region; and initiatives by governments to cultivate and develop partnerships.

adenovirus vaccine platform in many jurisdictions, there were no patents (granted or pending) in Argentina or Brazil, the LAC countries where drug substance production was located. VaxPaL, a database of patent landscapes for COVID-19 vaccines, reports nothing in Argentina and one application in Brazil ("Simian adenovirus and hybrid adenoviral vectors") that was filed in 2012 but is recorded as withdrawn. VaxPaL also reports another application for this vaccine that was filed in Mexico in 2019 but without a recorded outcome ("Method for generating a recombinant adenovirus comprising a nucleotide sequence encoding a heterologous gene of interest for use as a vaccine"). VaxPaL, www.vaxpal.org/?originator%5B%5D=AstraZeneca&originator%5B%5D=Oxford+University&countries%5B%5D=Argentina&countries%5B%5D=Brazil&countries%5B%5D=Mexico&page=1 (last visited Feb. 16, 2023).

[86] Veronica Vargas, Martin Rama & Rucheta Singh, *Pharmaceuticals in Latin America and the Caribbean: Players, Access, and Innovation across Diverse Models*, Open Knowledge Repository Beta (2022), https://openknowledge.worldbank.org/handle/10986/36871 (last visited Dec. 7, 2022).

Local and regional production of the type discussed in this chapter cannot advance in the absence of the originators being willing to transfer the essential technology, know-how, and data that they possess. Realizing the potential benefits derived from working with originators, discussed in the previous section, depends on originators having both the desire and means to collaborate with local partners. The inclusion of "means" is important, for, as was the case with the Cuban vaccines (and also the Texas Children's Hospital's vaccine), even originators that express desire to transfer technology may face resource constraints that limit their abilities to do so.[87]

Among originator firms with the resources, we know little about why vaccine developers pursued different approaches to scaling up production. What we do know, however, is that AstraZeneca stands out, with a commitment to decentralized and "distributed" production based on transferring technology, know-how, and data to partners across the globe, and, importantly, dedicating resources to help this to proceed quickly. Had more companies adopted similar postures on their own or been encouraged to do so with appropriate incentives and instruments, there likely would have been more cases of technology transfer than those covered in this chapter. Ultimately, understanding originator companies' differing approaches to technology transfer and the construction of global manufacturing networks for COVID-19 vaccines is a crucially important area that demands additional research.

As importantly, more research is also needed to understand better the appropriate set of instruments to encourage such behavior. Proposals to compel, mandate, or force the sharing of technology, know-how, and data are common, but this is easier said than done. Researchers need to think carefully about what national and international actors can effectively achieve in this regard. This could include more explicit conditions attached to research funding and strategic use of purchasing that rewards producers for meeting output targets that could only be achieved by engaging in wider technology transfer.

The existence of local partners with sufficient capabilities of course matters too. Even without fully understanding originators' strategies, and accepting that some international firms simply did not prioritize or were not interested in producing in Latin America and the Caribbean (and were not adequately incentivized to do so), it is reasonable to expect that firms that were prepared, in principle, to transfer technology would only do so with partners possessing adequate capabilities. As it happened, partnerships tended to be located in the countries with the largest pharmaceutical sectors, with the most advanced technological and production capabilities. This is not surprising, and points to the importance of legacies of development in national pharmaceutical industries. Consider the case of Argentina, where the August 2020 announcement of the AstraZeneca production

[87] Contreras & Shadlen, *supra* note 51. This appears to be relevant for Sputnik-V too, where the substantial announcements of technology transfer were rarely accompanied by sufficient delivery of the necessary expertise.

arrangement involving mAbxience was celebrated as validation of the country's scientific community.[88] This outcome was not just made possible by the country's strong science base, but, specifically, a strong pharmaceutical industry, as it is the existence of the *manufacturing* firm that allowed this to happen: firms like mAbxience not only are staffed by highly qualified scientists and technicians, but they possess the industrial and management capabilities that enable engagement with originators. Indeed, this is precisely what the then head of AstraZeneca for the Southern Cone said at the time of the announcement in August 2020: "This agreement highlights our country's great level of professionals, quality of science, and *production capabilities*."[89]

Could more LAC firms have become engaged? The universe of potential partners for technology transfer and production, though not infinite, almost certainly exceeds the handful of firms that have been discussed in this chapter. Lists of firms with approved biological products, for example, a useful indicator of capacity to manufacture vaccines, includes many companies that have not been mentioned here.[90] In 2021, Argentina's Ministry of Productive Development undertook a survey of biological production capabilities in the pharmaceutical industry, reporting seven firms producing the active ingredients for injectable biological products that could contribute to vaccine production.[91]

Capabilities is not a binary category, however, something that companies either have or do not have, but rather sets of attributes that exist in varying degrees. Nor are the same capabilities equally important for producing all vaccines. Even for the same vaccines, firms that participated in COVID-19 production partnerships did so with different levels of capabilities; mAbxience needed less technical assistance from AstraZeneca to make the drug substance than BioManguinhos did, for example. It is difficult to identify and measure what level and type of capabilities are needed, and which firms have those specific capabilities. Yet it is reasonable to conclude that there are plenty of LAC firms with latent capabilities that, with the engagement of

[88] The head of science at *La Nación* wrote: "Moments like this, when we manage to secure technology transfer for a coronavirus vaccine to be produced in the country, this is the answer to those who wonder what the purpose is of state investment in training scientists." Nora Bär, *Vacuna de Oxford en la Argentina: Un Logro que se Nutre de la Capacidad Científico-tecnológica Local*, La Nación (Aug. 13, 2020), www.lanacion.com.ar/ciencia/vacuna-oxford-argentina-logro-se-nutre-capacidad-nid2419601/ (last visited Dec. 7, 2022).

[89] *La Argentina Fabricará una Vacuna*, *supra* note 57 (emphasis added). It is worth underscoring that transnational pharmaceutical firms praising and celebrating the extent of local Argentinean firms' production capabilities is a rare phenomenon.

[90] Vargas, Rama & Singh, *supra* note 86; Similar biotherapeutic products approved and marketed in Latin America, www.gabionline.net/biosimilars/general/similar-biotherapeutic-products-approved-and-marketed-in-latin-america (last visited Dec. 7, 2022); Vargas, *supra* note 43.

[91] Document on file with the author. For an extensive examination of biopharmaceutical production in Argentina, see Explorando el Camino de la Imitación Creativa: La Industria Biofarmacéutica Argentina en Los 2000 (Pablo Lavarello, Graciela Gutman & Sebastián Sztulwark eds., 2018).

originators, could be useful partners. As an illustration, consider that Richmond, which partnered to produce Sputnik-V and is now collaborating with CanSino, was not one of the firms mentioned in the Argentinean government's survey of biological producers in Argentina – though it almost certainly would be now, were another landscaping exercise of this sort to be undertaken.

Of course, not all potential local partners are interested. That BioManguinhos would participate in the venture with AstraZeneca is unsurprising; this is what it does. BioManguinhos is a public lab that engages in technology transfer to produce vaccines and other biological products for Brazil's Ministry of Health, and it actively prospected for technology transfer partners.[92] The interest of private firms is more variable. mAbxience and Liomont had new facilities that were available and saw opportunities to seize; likewise União Química and Richmond regarded collaboration to manufacture Sputnik-V as a point of entry into the world of vaccine production. Not all potential partners found themselves in such a position, able and willing to use production capacities for available facilities.[93]

This brings us to the issue of government initiatives to establish partnerships. In Brazil, BioManguinhos and the Ministry of Health worked together to advance the technology transfer arrangement with AstraZeneca, while the production of Sinovac emerged from the initiative of Butantan working with the government of the state of São Paulo. In no other LAC country are such active steps to identify partners and generate partnerships evident, and in Brazil the laboratories most involved in COVID-19 vaccine production are part of the public sector. In Argentina and Mexico, although the arrangement involving mAbxience and Liomont was celebrated by both governments, it was not driven by the governments but rather AstraZeneca and the Slim Foundation. Likewise, Richmond's venture to produce Sputnik-V, though receiving public funding, came about through its own initiative.

It is possible that public actors, LAC governments or the Pan-American Health Organization, could have done more to increase the participation of local firms in vaccine production. This might have taken multiple forms. With regard to firms that possessed the requisite (or latent) capabilities but were not interested, with the right incentives these could potentially have been motivated to participate. More ambitiously, and analogous to what was witnessed in the United States and United Kingdom, where government officials regarded vaccine development *and local manufacture* to be a high priority and engaged with private firms in new ways,[94]

[92] Indeed, prior to the pandemic, BioManguinhos already had a prospecting unit with a mission to identify and evaluate technology transfer projects.

[93] In discussions of local fill–finish of the AstraZeneca vaccine in Argentina, for example, Biogénesis Bagó, one of the firms mentioned as a possible producer, is a key supplier of vaccines for animal health (foot-and-mouth disease), not just for Argentina but throughout the region. Could this firm have produced COVID-19 vaccines while also maintaining production of the veterinary vaccines?

[94] Sampat & Shadlen, *supra* note 48.

governments of LAC countries with large pharmaceutical industries could potentially have contacted foreign originators (and the governments and international organizations sponsoring some of the originators) in efforts to broker deals. Consider again the arrangements for the AstraZeneca vaccine to be produced in Argentina and Mexico. An Argentinean partner could have been engaged originally for the fill–finish stage – not somehow mobilized on an emergency basis as an afterthought in 2021, which was proposed but infeasible for the reasons discussed in Section 2, but included in the original design of the agreement in 2020. One reason given for the binational arrangements including a Mexican partner is that this was a condition of the Slim Foundation's financing, but that only begs the question of why philanthropic resources played such an important role, presupposing the Slim Foundation's involvement. Could, potentially, the Argentine government have made this happen, working directly with AstraZeneca (and other originators) and national firms? More generally, and beyond Argentina per se, might governments have been able to do more to make production partnerships come to fruition, exploiting existing and latent capabilities in their pharmaceutical industries and providing the incentives to entice partners? Future research should explore how governments in countries with large pharmaceutical industries can leverage local capabilities to attract originators and foster technology transfer agreements.

Going forward, one way to make more partnerships more likely is to have more potential local partners. To that end, LAC governments and regional organizations, regarding the paucity of local manufacture of COVID-19 vaccines as a source of vulnerability that must not be allowed to repeat, appear to be investing in pharmaceutical production capabilities.[95] LAC firms are also involved in the WHO's mRNA vaccine program.[96] Initiatives to increase local production are not just for vaccines, but the full range of essential medical countermeasures, including treatments, diagnostics, oxygen, personal protective equipment, and so on. While a full review of these efforts is beyond the scope of this chapter, what they have in common is that they are directed toward decreasing the region's heavy dependence on imports, which has come to be regarded as an Achilles' heel, a dangerous source of vulnerability to be addressed.

[95] Luke Taylor, *Covid-19: Latin America Must Reduce Its Reliance on Medical Imports*, 380 BMJ 576 (2023); PAHO, *supra* note 4; PROSUR, *supra* note 4; ECLAC, *supra* note 4.

[96] *PAHO Selects Centers in Argentina, Brazil to Develop COVID-19 mRNA Vaccines*,– PAHO/WHO | Pan American Health Organization (Sep. 21, 2021), www.paho.org/en/news/21-9-2021-paho-selects-centers-argentina-brazil-develop-covid-19-mrna-vaccines (last visited Dec. 7, 2022); *Unseating Big Pharma: The Radical Plan for Vaccine Equity*, NATURE (Jul. 13, 2021), www.nature.com/immersive/d41586-022-01898-3/index.html (last visited Nov. 8, 2022).