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Inequity in access to vaccines: the failure of the global response to the COVID-19 pandemic

Desigualdad en el acceso a las vacunas: el fracaso de la respuesta mundial a la pandemia de COVID-19

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ABSTRACT This article summarizes the strategies used to rapidly develop COVID-19 vaccines and distribute them globally, with an emphasis on vaccines developed in western nations. It is based on interviews and information gathered regarding the response to the pandemic, both from international organizations and official documents from Brazil, Argentina, Colombia, Peru, and Mexico. While vaccine development has been hailed as successful, their global distribution has been highly unequal. We look at how the pandemic succeeded in mobilizing large quantities of government resources, and how citizens volunteered their bodies so that clinical trials could be completed quickly. However, patents prevented the expansion of manufacturing capacity, and the governments of a few wealthy countries prioritized the protection – and in some cases overprotection – of their citizens at the expense of protecting the rest of world's population. Among the major beneficiaries of the global response to the pandemic are the leading vaccine companies, their executives, and investors. The article concludes with some of the lessons learned in this process.
KEY WORDS Vaccines; COVID-19; Global Health; Delivery of Health Care.

RESUMEN Este artículo resume las estrategias que se han utilizado para desarrollar rápidamente las vacunas COVID-19 y distribuirlas a nivel mundial. Se centra en las vacunas desarrolladas en los países occidentales. Con base en entrevistas y recopilación de información existente sobre la respuesta a la pandemia, tanto de agencias internacionales como de documentos oficiales de Brasil, Argentina, Colombia, Perú y México se reconoce que, si bien el desarrollo de las vacunas ha sido un éxito, su distribución a nivel mundial ha sido muy desigual. Como veremos, la pandemia consiguió movilizar una gran cantidad de recursos gubernamentales y los ciudadanos prestaron sus cuerpos para que los ensayos clínicos se pudieran concluir rápidamente. Sin embargo, las patentes impidieron la expansión de la capacidad de fabricación y los gobiernos de unos pocos países ricos priorizaron la protección y, en algunos casos, la sobreprotección de sus ciudadanos a expensas de la protección del resto de la población mundial. Entre los principales beneficiarios de la respuesta mundial a la pandemia se encuentran las principales empresas de vacunas, sus ejecutivos e inversores. El artículo concluye con algunas de las lecciones aprendidas en este proceso.
PALABRAS CLAVES Vacunas; COVID-19; Salud Global; Atención a la Salud.

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INTRODUCTION

On January 11, 2020, the World Health Organization (WHO) declared the coronavirus (COVID-19) outbreak a global pandemic. By the end of April 2022, nearly 6.2 million deaths and 507 million COVID-19 infections had been reported, in addition to a large but unknown number of asymptomatic cases, millions that were diagnosed but not reported, and probably many more that were not diagnosed. There is no doubt that this pandemic has been the greatest public health challenge that international agencies and governments have faced in recent decades, and it has had medical, social, and economic consequences rarely experienced.

The governments of China, Russia and the USA decided that the most expeditious response to the pandemic was to develop as quickly as possible a vaccine capable of reducing the severity of infections and curbing their transmission. To this end, regulatory agencies adjusted their procedures, breaking with the scientific canons established over time, and governments invested large amounts of money in funding vaccine research and development (R&D) and in broadening the manufacture capacity. At the same time, international agencies established programs to promote an equitable global distribution of vaccines, under the premise that in a globalized world no one would be safe until everyone was vaccinated.

ABOUT THIS STUDY

This article is based on fieldwork and on the collection of existing information regarding the response to the COVID-19 pandemic, from its start in January 2020 until April 2022. A narrative review of published articles, programs and orientations for managing the pandemic provided by international agencies was carried out, with an emphasis on health agencies – such as the Pan-American Health Organization and the World Health Organization – and the World Trade Organization. Official documents from Brazil, Argentina, Colombia, Peru and Mexico were also reviewed.

The fieldwork consisted of interviews with members of regulatory agencies, research ethics committees, researchers and study participants of the Janssen vaccine study in Latin America, in addition to Internet conversations with consumer defense groups.

After analyzing the strategies used to rapidly develop the vaccines, we described the plans established to achieve worldwide distribution and analyzed the factors and actors that prevented the protection of the global population. Throughout the text, we point out the ethical questions raised by the strategies used to develop and distribute the vaccines.

RAPID DEVELOPMENT AND APPROVAL OF COVID-19 VACCINES: THE CONSEQUENCES

Biotech companies and government research centers developed COVID-19 vaccines in record time.[1] Sputnik, a Russian vaccine, was the first to be widely used, and it was approved without having conducted Phase 3 studies.[2] It was rapidly followed by a vaccine made in China.

It is conceivable that the US, seeking to demonstrate that its scientific capacity was not inferior to that of its two archenemies did not want to be left behind, and gave *carte blanche* to its regulatory agency, the Food and Drug Administration (FDA), to grant ultra-rapid approvals to the COVID-19 vaccines being developed. In 2020, President Donald Trump was running for re-election and did not want the pandemic to thwart his chances, so his administration granted multi-million-dollar awards to innovative pharmaceutical companies and pressured the National Institutes of Health (NIH) to support the required research. Even after the election, President Trump continued to pressure federal

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scientists and told the FDA director that he could be dismissed if he did not approve vaccines within the next 48 hours.[3]

Prior to the COVID-19 pandemic, no vaccine had been developed in less than four years and some took decades.[4] Ken Frazier, former Merck CEO, suggested in a July 2020 interview that it was not possible to do it in less than four years:

> In the last quarter century, there have only been seven, truly new vaccines introduced globally at the clinical practice. When I say new, that means that they were effective against a pathogen for which there had previously been no vaccine. There are only seven in the last quarter century, Merck has four, the rest of the world has three. I don't mean to boast.[5]

In this case, Ken Frazier was wrong. Some of the COVID-19 vaccines were developed and approved in less than a year and, as we shall see, in less than two years the WHO had approved 11.

The confluence of several factors facilitated such rapid vaccine development in the US and elsewhere, including:

1) Research on coronaviruses and viral vaccines had been underway for years.[1]
2) The severity of the prognoses for the economy and for the health system, as well as the absence of adequate treatments, put pressure on the regulatory agencies, leading to modifications in the research and development (R&D) processes, for example, starting advanced clinical trials phases without having the results of earlier phases, or conducting them in parallel. There was a plethora of volunteers to participate in clinical trials, so recruitment was very rapid, and emergency use approvals were issued before the completion of vaccine safety and efficacy trials.
3) Governments provided large amounts of funding for vaccine development to both public and private companies.
4) Government investment in advance purchase commitments.

Regulatory changes

On December 2, 2020, British regulators authorized the Oxford and AstraZeneca's vaccine for emergency use, seven months after the start of the clinical trials.[6] Similarly, the speed with which the FDA approved the vaccines broke historical records. The Pfizer and Moderna vaccines were approved for emergency use on December 11 and 18, 2020, respectively, less than a year after the clinical trials had been started. Johnson and Johnson submitted the Sponsor Briefing Document to request the FDA's approval of its vaccine on February 26, 2021.[7] Two days later it was cleared for emergency use, and it was launched on March 1. With this vaccine, as with others, the Phase 3 trial was started before completing the analyses of the results of the first two phases,[7] a fact that escaped the scrutiny of the Research Ethics Committees, some investigators, and the participants in the ENSEMBLE clinical trial, as that information was not included in the informed consents.[8]

On January 3, 2021, the Covaxin vaccine was approved in India, before the completion of the clinical trials.[9] Covishield, the first Indian vaccine against COVID-19, was not developed as quickly, but the regulatory agency approved it for emergency use on the same date.[10] Some Indian scientists expressed astonishment at the speed with which vaccines were being approved in their country. Asked what the new norms meant, Dr. Gagandeep Kang, one of the best-known vaccine experts and vice president of Coalition for Epidemic Preparedness Innovations (CEPI) said, "I have no clue. I have never seen anything like this before... Either you are doing a clinical trial, or you are not. I am confused." suggesting that using shortcuts in clinical experimentation could have undesirable consequences.[11]

Russia and Cuba, after testing vaccines in a very small group (phase 1), skipped phases 2 and 3, and with limited information

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proceeded to vaccinate the population. As they administered vaccines, they learned about their efficacy and safety. We do not know if the participants in these population-based experiments received the necessary information to consent freely and consciously to receive the experimental vaccines and accept the risks and benefits they entailed.

Less than a year after unveiling the virus genome, that is in the late 2020 and early 2021, the regulatory agencies of most Western and other countries had authorized one or more vaccines for emergency use. By September 7, 2021, WHO had granted licenses for emergency use to six vaccines and by March 2022 it had approved 11, including one from India. Considering that in addition to India, Cuba has produced three vaccines, which WHO has not yet approved, it has been proven that not only high-income countries can produce vaccines. Recently, two professors from Texas Children's Hospital developed a vaccine that has been approved in India[12] and Botswana,[13] but not by the FDA or the WHO.

There is no denying that vaccines' approval by the regulatory agencies has had certain political undertones. For example, until now, the FDA has only approved three vaccines developed by three pharmaceutical companies: two of vaccines are from the two largest US pharmaceutical companies (Johnson & Johnson and Pfizer) and the third (Moderna) was developed with the financial support of the federal government and in collaboration with researchers from the National Institutes of Health. As will be discussed, the US government has asserted that it can claim a patent interest in Moderna's vaccine because it contributed to its development.

The FDA has not approved any of the other WHO-approved vaccines developed in Russia, China, and India, the country that has produced the most vaccines. Nor has it approved the vaccine developed by Oxford University, with funding from the British government, and transferred to AstraZeneca, the European company that conducted the clinical trials and marketed the vaccine. The latter has been approved by the European Medicines Agency (EMA) and by the WHO. It is difficult to believe that the FDA's decision responds to a genuine desire to choose the best vaccines, because not long ago it was disclosed that the efficacy of the Johnson & Johnson vaccine is only 52%.[14]

The number of subjects who have participated in the various COVID-19 vaccine trials has been less than half the number of the enrollees historically used in vaccine studies, rarely exceeding 45,000, in some cases limited to about 20,000 and in the case of the Texas vaccine to 3,000. The small sample size and the availability of many volunteers, predominantly health care workers and people whose jobs put them at high risk of infection, expedited the recruitment process, which is usually the most time-consuming part of a clinical trial.[15]

Significant public funding

Some governments, including the US and the UK, have granted enormous amounts of public funding to public research centers, universities, and private companies, facilitating the R&D processes. In the case of the Oxford-AstraZeneca vaccine, 97% of the funding was public. In India, the Covaxin vaccine developed by Bharat Biotech was fully funded by the public sector,[16,17] and the Serum Institute of India and Bharat Biotech received US$610 million from the government to boost production capacity.[18]

The amount of public resources provided by the governments of Russia, China and Cuba is unknown, but the speed with which Russia and China developed their vaccines indicates that they started investing in their development early on. Cuba developed and applied three vaccines: Soberana 02, Soberana Plus and Abdala.[19] In early January 2022, after these vaccines had been developed and used, the Banco Centroamericano de Integración Economica approved a loan of €46.7 million for "the development of vaccines."[20] It is understood that this loan will be used to modernize the technology and

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increase the production of vaccines, antibiotics, biosimilars and other pharmaceutical products.[20]

It is safe to say that the public sector has been, from the start, the main funder of the R&D of most vaccines, with the exception of the Pfizer vaccine.

The U.S, through the Biomedical Advanced Research and Development Authority (BARDA), the Assistant Secretary for Preparedness and Response (ASPR), the National Institutes of Health (NIH), and advance purchase commitments (see below) have helped all US pharmaceutical companies develop and/or produce approved vaccines. There is no precise estimate of what the US government has spent because it has been funding for years the basic research that has allowed the rapid progress in vaccine development.

The Congressional Budget Office has estimated that BARDA alone invested US$19.3 billion in vaccine development.[21,22] This includes funds allocated to companies, US$2.5 billion to Moderna, US$500 million to Johnson & Johnson, US$1.6 billion to Novavax to expand manufacturing plants, and advance purchase commitments that allowed companies to start manufacturing with low risk. As we shall see, advance purchase agreements were also established with Pfizer and Moderna. The Biden administration has continued to fund the purchase of the vaccines to be distributed within the country and reached an agreement with Merck to repurpose two of its facilities for the rapid large-scale manufacturing of the Johnson & Johnson (Janssen) COVID-19 vaccine.[23]

However, companies that have received public funding and scientific support for vaccine development have not always shared the profits from their sales with taxpayers. For example, in the case of the Moderna vaccine, Dr. Francis Collins, then director of the US National Institutes of Health (NIH), reported that judges will have to decide who is the inventor of the NIH-Moderna COVID-19 vaccine. Echoing his communication, Peter Maybarduk, director of Public Citizen's Access to Medicines Program, wrote to Dr. Collins suggesting that the US government might take Moderna to court because the company had failed to list the NIH as the inventor of the vaccine when applying for patents:

> The US government is showing a modicum of verve at last, suggesting it will not allow federal scientists' role in the invention the of the NIH-Moderna vaccine to be erased. Recognition as the vaccine's joint inventor can help the US government finally responsibly steward the vaccine's use, including by helping secure access for the billions of people still awaiting a safe path out of the pandemic [...] We, the people, paid for its development. Federal scientists pioneered the understanding of coronaviruses and then worked in partnership with Moderna.[24]

However, "in an August statement to the US Patent and Trademark Office, Moderna acknowledged that the NIH had submitted three of its researchers as co-inventors, but stood by its decision to exclude them from the application."[6]

The same question is being raised in India: shouldn't the patent for the vaccine that has been developed with public money belong to the government?[16]

Advance purchase commitments

The purpose of advance purchase commitments is to advance cash so that companies can start manufacturing the vaccines under development as soon as possible, even before receiving regulatory approval. This is important because when there is an epidemic, the use of vaccines can break the chain of transmission of microorganisms, and they must be administered as soon as possible. When companies, with or without government assistance, accumulate large quantities of vaccine candidates without knowing their effectiveness or safety, they run the risk of losing their investment, as would happen if clinical trials failed and/or the regulatory authority failed to approve the vaccine. The investment can also be lost, in whole or in part, when the

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regulatory authority requires changes or a new clinical trial and delays product approval, as the existing stock could expire before the vaccines are applied.

The advance purchase commitments established by the US government with US-based companies allowed the latter to manufacture of millions of vaccine candidates so that they would be ready for distribution upon regulatory approval. The advance commitment to purchase 100 million doses allowed Johnson & Johnson to begin distributing its vaccine on March 1, 2021,[25] three days after receiving the FDA authorization for emergency use. The government also pre-purchased the same number of vaccine doses from Moderna[26] and Pfizer.[27]

In July 2020, nearly six months before the FDA approved the Pfizer's vaccine for emergency use – the first vaccine to be approved in the US – the US government agreed to a purchase of 100 million doses. The secretary of the Department of Health and Human Services (DHHS) and the company have contradicted each other in explaining whether Pfizer did not accept a second purchase offer or whether the government did not want commit without ensuring that the company could deliver an additional 500 million doses.[27] The United Kingdom also hoarded vaccine doses produced by Oxford-AstraZeneca to vaccinate its population, and in July 2020 it purchased 90 million doses.[28]

Some analysts have criticized the advance purchase commitments and they have labeled them as "vaccine nationalism."[29] Advance purchase commitments have to be established so that the necessary vaccines to control viral transmission are available as soon as possible. However, this decision cannot be considered acceptable or ethical if a few countries use advance purchases to monopolize all vaccines and leave a significant percentage of the global population without access to them, as has happened. The problem is not the advance purchase commitments but the way they have been executed.

Advance purchase commitments would have been ethical if all countries had been able to access the vaccines, in accordance to pre-established prioritization criteria based on the risk of experiencing severe events and the probability of limiting transmission, for example, people who provide basic services (health, education, emergency response), those who are in continuous contact with other people, the elderly, and the immunocompromised. It has been said that in order to control the pandemic, 75% of the global population has to be effectively vaccinated. In this context, "effectively" means that one needs to take into account that not all vaccines are 100% effective.

In summary, through emergency use approval, public funding, and advance purchase commitments, governments reduced the risks typically faced by companies engaged in vaccine development; the companies had an assured demand, a decrease in development costs, and a significant reduction in the time to develop, produce, and sell the product.[22]

Consequences of ultra-rapid vaccine development

Such rapid vaccine development meant that people started to be vaccinated with insufficient knowledge about the safety and efficacy of the vaccines, especially for important subgroups of the population. It also forced researchers to unblind clinical trial participants as vaccines became available. The lack of information about adverse effects, their duration and severity are especially serious when the vaccine development process is new, as is in the case of mRNA vaccines that instruct our cells to produce a protein that triggers an immune response within our body, a technique that so far has only been used in the Ebola vaccines that have been administered to a very small number of people. Among other unexpected adverse events, lymphadenopathy, syncope, paresthesias, myocarditis, Bell's palsy, and most recently tinnitus has been reported,[30] and new adverse events, some of which may be permanent, continue to be documented. Adenovirus vaccines have produced cases of thrombosis with

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thrombocytopenia, Guillain Barré syndrome, and tinnitus.[30]

The duration of vaccine protection provided and their protection against new mutations of the virus is also unknown, as well as the need and convenience of third, fourth or future boosters. For example, it is known that the protection from infection wanes at 12-16 weeks for both Delta and Omicron variants,[31,32,33,34,35,36,37] and in the case of the Oxford-AstraZenca vaccine it virtually disappears.[38]

It is hard to understand why, given the novelty of mRNA vaccines – only licensed for emergency use – and the insistence of governments to vaccinate the entire population, no effective tracking and rapid adverse event reporting system was developed. Such a system would have allowed for the identification of immediate adverse events following vaccination as well as those that might appear in the longer term. In the US, neither the Centers for Disease Control and Prevention (CDC) nor the FDA has established rigorous pharmacovigilance programs, missing a major opportunity to document in detail the safety of these vaccines; part of this failure may be attributable to the political situation. The FDA did not have a permanent director during most of 2021.

The emergency use authorization of the first COVID-19 vaccines was based on the preliminary results of clinical trials, most of which would not be completed for months and some of which (for example, Moderna and Johnson & Johnson) are yet to be completed. This circumstance generated an ethical conflict. In the presence of authorized vaccines, it was unethical to continue to expose clinical trial participants to the risk of infection, especially those in the placebo group. This circumstance had not been foreseen in the research protocols since there had never been so many vaccines being developed against the same pathogen in so many different countries. Consequently, the companies faced the ethical imperative to unblind the clinical trial participants so that those enrolled in the placebo group could be vaccinated. In most cases, the blind was opened as participants became eligible to receive the vaccine offered by government to the residents of their country, and participants could frequently choose between receiving the government offered vaccine or the vaccine tested in the clinical trial in which they were enrolled.

In other words, the placebo groups disappeared, and practically all participants received the vaccines they were able to access, which could vary from country to country or among participants in the same country. For example, in Peru, when the blind of the Johnson & Johnson vaccine trial was opened, those in the placebo group received the Sinopharm vaccine, which was not used in Mexico or Colombia, where the same trial was conducted. In Colombia some participants received the Sinovac vaccine, regardless of whether they had been in the experimental or placebo group, and others received the Johnson & Johnson vaccine.[8] Apart from these problems and protocol deviations that will undoubtedly complicate the analysis of the final results, the unblinding of the study participants may distort the nature of the trial and bias the investigators.[39,40]

Contractual arrangements

Some of the contractual conditions that US pharmaceutical corporations have imposed on governments are abusive. Zain Rizvi obtained unredacted contracts and published detailed examples of the conditions included in Pfizer's contracts.[41] According to the introduction, "the contracts offer a rare glimpse into the power one pharmaceutical corporation has gained to silence governments, throttle supply, shift risk and maximize profits in the worst public health crisis in a century." [41]

The contracts, even those with the US and the European Union, included nondisclosure agreements precluding governments from announcing the existence of the agreements, the terms, the transactions and the relationship between Pfizer and the respective governments.

Pfizer precluded Brazil from receiving or donating COVID-19 vaccine doses to other

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countries. "If Brazil were to accept donated doses without Pfizer's permission, it would be considered an 'uncurable material breach' of their agreement, allowing Pfizer to immediately terminate the agreement" but Brazil would have to pay for the remaining orders.[41]

At least four countries are required:

> "to indemnify, defend and hold harmless Pfizer" from and against any and all suits, claims, actions, demands, damages, costs, and expenses related to vaccine intellectual property. For example, if another vaccine maker sued Pfizer for patent infringement in Colombia, the contract requires the Colombian government to foot the bill. At Pfizer's request, Colombia is required to defend the company [...] Pfizer also explicitly says that it does not guarantee that its product does not violate third-party IP [intellectual property], or that it needs additional licenses.[41]

All contractual disputes must be resolved through arbitration, not through the courts. Moreover, in the case of Albania, Brazil, Chile, Colombia, Dominican Republic, Peru and most likely other countries that Rizvi was unable to investigate, "contractual disputes [are] subject to International Chamber of Commerce arbitration applying New York law."[41] Private arbitration allows corporations to bypass domestic legal processes.

Brazil, Chile, Colombia, the Dominican Republic, and Peru had to waive sovereign immunity:

> In the case of Brazil, Chile and Colombia, for example, the government "expressly and irrevocably waives any right of immunity which either it or its assets may have or acquire in the future" to enforce any arbitration award. For Brazil, Chile, Colombia, and the Dominican Republic, this includes "immunity against precautionary seizure of any of its assets."[41]

A report of the Bureau of Investigative Journalism explains that Pfizer demanded from several Latin American countries:

> ...indemnity from civil cases, meaning that the company would not be held liable for rare adverse effects or for its own acts of negligence, fraud or malice [...] This includes those linked to company practices – say, if Pfizer sent the wrong vaccine or made errors during manufacturing.[42]

Georgetown Law professor Lawrence Gostin added that "some liability protection is warranted, but certainly not for fraud, gross negligence, mismanagement, failure to follow good manufacturing practices."[42]

In Colombia, Janssen, a subsidiary of Johnson & Johnson, among other things demanded that the Government sign a "Confidential Disclosure" forbidding the government from revealing the price of the vaccines. The violation of this agreement:

> ...would constitute a revelation of confidential information, implying a contractual violation, and consequently fines and sanctions. At the same time, it will carry the risk of unilateral suspension of commercial agreements with the government of Colombia regarding the delivery of the Coronavirus Sars-CoV-2 (COVID-19).[43]

Programs to achieve global vaccination

In a globalized world, where the movement of people and goods is continuous and rapid, it is difficult to interrupt viral transmission if the entire world population does not have access to effective vaccines. The longer it takes to vaccinate everyone, the greater the number of infections, deaths, and virus mutations. To achieve global vaccination, a series of international programs have been established and evaluated by Bermudez and Bermudez[44] and the Dutch organization Wemos.[45] They are summarized in Table 1.

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Table 1. Global programs to facilitate access to COVID-19 vaccines, 2020-2021.

Name	Description	Aims and performance
COVAX (April 2020)	Covax is part of the ACT Accelerator (Access to COVID-19 Tools Accelerator) initiative launched by WHO with the support of more than forty countries and organizations. It brings together governments, scientists, civil society, philanthropic foundations, companies, and global health organizations. The goal of the ACT Accelerator is to support the development and equitable distribution of medicines, vaccines, and other essential tools to combat COVID-19. The ACT Accelerator was organized along four main axes: diagnostics, treatment, vaccines, and health systems strengthening. The vaccine axis is known as COVAX, and is responsible for stimulating production, purchasing, and distributing vaccines worldwide. COVAX, which is led by CEPI (Coalition for Epidemic Preparedness Innovations), GAVI (Global Alliance for Vaccines and Immunizations), WHO, and UNICEF, contributes to vaccine delivery.[46]	COVAX sought government and private sector commitments valued at $18.9 billion, either in cash or in-kind, to deliver vaccines for 20% of the world's population, but it failed. By October 2021, only US$4.7 billion had been raised.[45] By the end of 2021, COVAX was expected to have delivered 2 billion vaccines, mainly to the 92 low- and middle-income countries. As this amount could not be achieved, the target was reduced to 1.4 billion. On January 15, 2022, it was announced that it had secured 1 billion doses. Covax has also invested US$1.2 billion in vaccine development.[45] Recently, an agreement was secured between Johnson & Johnson and COVAX to distribute 300,000 doses of its vaccine through UN peace operations in war areas.[47] An achievement that cannot be considered significant because the US CDC has recommended that this vaccine be discontinued due to safety concerns.[48] It can be concluded that COVAX is not an initiative that will have the impact that was expected.
Team Europe (April 2020)	Led by the European Union and its member states in collaboration with the European Investment Bank and the European Bank for Reconstruction and Development. It is expected to have €46 billion at its disposal.	Its aim is to work primarily with low- and middle-income countries to combat COVID-19 and help in recovery efforts. Its goal is to vaccinate 70% of the population by mid-2022, through vaccine donations and financial support to increase the manufacturing capacity of medical products.[45] As of February 2022 alone, they have contributed €3 billion to COVAX. It has also donated vaccines directly to low- and middle-income countries and contributed €1 billion to increase local production of vaccines, drugs and other medical technologies.[45]
C-TAP (May 2020)	Aiming to produce the number of vaccines globally needed, the WHO, at Costa Rica's suggestion, established the C-TAP technology bank,[49] which now has the support of many other States. C-TAP aims to promote the exchange of information, data, knowledge, and other resources to accelerate the development of products needed to combat the pandemic.	However, so far it has not licensed any vaccines, only recently has entered into a licensing agreement with Merck to facilitate the production of molnupiravir by other manufacturers. Recent clinical trials of molnupiravir have shown very limited benefits in the treatment of COVID-19 and serious adverse effects.[50] In other words, C-TAP has failed to obtain the open licenses needed to scale up production of COVID-19 medical technologies.[51] Surprisingly, Pfizer has shared its nirmatrelvir patents (PAXLOVIDD PF-07321332) with the UNITAID Patent Bank. The FDA cleared the emergency use of this drug in combination with ritonavir to treat COVID-19. On March 9, 2022, the company announced that it was initiating the clinical trial in non-hospitalized pediatric patients over 12 years of age.[52]
G20 High-Level Independent Panel (HLIP) (January 2021)	Its objective is to establish a reliable and sustainable financing mechanism of the global commons for pandemic prevention, preparedness and response. HLIP members are predominantly experts in economics and finance, and serve in their individual and independent capacity. This panel has called for US$75 billion in international public funding. One of this panel's proposals is the creation of a Global Health Threats Fund financed by pre-agreed contributions from governments, which would be established as an intermediary financial fund at the World Bank. The governance of the fund would be independent of the World Bank and governed by a board whose role would be to determine the priorities of the fund. This initiative is expected to mobilize between US$5 billion and US$10 billion annually, over a period of 10 to 15 years.[53]	It is difficult to imagine how in 2021, they can have all the necessary information to be able to cost alternative strategies to manage the next pandemic. One might think that the costs would be very different if vaccine patents were waived; or if new vaccines were discovered and produced in third world countries sold at modest prices or as they intend to do with the vaccine developed in Texas, and as the University of Oxford had wanted to do with its vaccine; or if the lessons learned during the management of the COVID-19 pandemic were taken into account. Whether the group of 20 nations will be willing to fund the suggested amount is unknown, considering that these are additional resources, and that so far these countries have contributed less than expected to international efforts to control the pandemic.
COVAX Manufacturing Task Force (May 2021)	It was established to identify and resolve issues impeding equitable access to vaccines through COVAX. It is co-led by: CEPI, WHO, UNICEF and Gavi. The collaborators are: the Bill & Melinda Gates Foundation, the International Federation of Pharmaceutical Manufacturers Associations (IFPMA), the Developing Countries Vaccine Manufacturers Network (DCVMN), and the Biotechnology Innovation Partnership (BIO).	The presence of collaborators with conflicts of interest calls into question whether decisions are aimed at solving the problems of low- and middle-income countries or at defending the interests of companies and their shareholders. The Gates Foundation is known for fiercely defending the patent system.[54] According to the Wemos assessment it does not have an overall business plan.[45]

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Table 1. Global programs to facilitate access to COVID-19 vaccines, 2020-2021 (continued).

Name	Description	Aims and performance
Multilateral Leaders Task Force on COVID-19 (June 2021)	Its goal is to urge the Group of 20 countries (G20) to fund various COVID-19 programs, including COVAX, and to donate one billion vaccines by 2021 to low- and middle-income countries. The World Bank, the International Monetary Fund (IMF), the World Trade Organization (WTO) and the WHO lead the group, although they do not contribute to directly fund any projects.	As it has been the case with the other programs, this group only managed to get 443 million doses donated in 2021. This program does not add anything to the other programs, and like the others it depends primarily on the goodwill of rich countries. It is understandable that, given the objectives of the World Bank, the IMF and the WTO, there is no mention of the need to break patents on vaccines and drugs that can reduce mortality and hospital stays.
European Health Emergency preparedness and Response Authority (HERA) (September 2021)	A program of the European Commission focused on the member countries of the European Union. It has a €30 billion budget, of which €24 billion come from other EU programs, to be used to fight COVID-19 and other health emergencies affecting the European Union.	Wemos[45] has described the problems with this program, which include the following: • These are funds that can be used, without any conditionality, to assist private companies in the development of vaccines, drugs and products needed to overcome a health emergency. • The HERA proposal has not been discussed by the European Parliament or among members of civil society, i.e. it is not a proposal that can be considered democratic. • The HERA program is not transparent, and the European Commission is not accountable to anyone. • Prior experience with the European Commission's advance purchase agreements casts doubt on price transparency and ignores the negative consequences they have had for low- and middle-income countries. • As a result of the dominant role of the pharmaceutical industry lobby in the Joint Industrial Cooperation Forum, pharmaceutical companies have played a prominent role in HERA, which has jeopardized public health interests..
IDA20 Regional Window 2021. IDA Private Sector Window (April 2021)	These are two World Bank programs and are managed by the World Bank's Board of Directors. They allow for the provision of loans to combat COVID-19 at a preferential interest rate. In addition, these loans are attached to requirements that can make them difficult to meet. .	The private sector program facilitates loans to companies that develop vaccines or drugs for low- and middle-income countries. This program is expected to increase the production of vaccines and remedies, but private companies would benefit the most, as they set the price for their products. .
South Africa COVID-19 mRNA Vaccine Technology Transfer Hub (mRNA hub) (June 2021)	WHO, The Medicines Patent Pool and the South African Consortium – comprised of the Southern African Biologics and Vaccines Institute (Biovac) and Afrigen Biologics & Vaccines, the South African Medical Research Council (SAMRC) and the African Centers for Disease Control and Prevention – collaborated to establish the first COVID-19 messenger RNA vaccine technology transfer hub (MRNAhub).[55] Of the proposed five-year budget of €92 million, they have raised €52 million. Afrigen Biologics & Vaccines will develop a permanent center for research, development, and production of mRNA vaccines, eventually to treat other diseases. The results of these activities will be of public domain and the technology will be shared with branches established elsewhere to produce and distribute the products in low- and middle-income countries. WHO has announced that the first branches will be in Egypt, Kenya, Senegal and Tunisia. .	If Pfizer and Moderna were to transfer the information necessary for vaccine production, their commercialization would be brought forward by possibly one year.[55] It appears that Moderna is now less resistant to sharing its information due to the public support it received to develop this vaccine and the pressure of the Biden administration. It is one of the most attractive solutions so far.

Source: Own elaboration from Wemos[45], World Health Organization[46], Pamuk[47], Romo y Henley[48], Worley[49], Lang[50], Onda Cero[51], Pfizer[52], Ravelo[53], Mookim[54], Infosalus[55].

Unfortunately, a large part of all these efforts have failed and 20 months after the beginning of the pandemic, it is estimated that only 57% of the global population is vaccinated.[56] Moreover, it must be considered that vaccine efficacy does not always reach 90% and, in some cases, it is limited to 60-65%.[57] We are far from controlling the COVID-19 pandemic through vaccine distribution. Furthermore, because vaccine effectiveness decreases over time, booster doses were recommended. During 2021, production was unable to meet the world's demand. Countries that subsidized the development of the vaccines and had the economic means were the first to receive the vaccines they had

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negotiated through advance purchase commitments, followed by high income countries. Less affluent countries were left behind. In January of 2022, WHO issued guidance on how to prioritize the worldwide distribution of COVID-19 vaccines in a fair manner,[58] but it was too late, and the roadmap was faulty.

Part of the problem is that the success of some of the initiatives, such as COVAX, C-TAP and the Multilateral Leaders Task Force on COVID-19 depends primarily on the goodwill of rich countries and companies.

We can conclude that, of all the initiatives mentioned, only the South Africa COVID-19 mRNA Vaccine Technology Transfer Hub (mRNA hub) is on track to achieve the proposed objectives.

Increasing vaccine production: the role of patents and the benefits for companies

One of greatest contributors to the inequitable access to vaccines has been the lack of installed capacity to quickly supply the world's population. As has been explained, the governments of high-income countries reacted to this reality by stockpiling vaccine doses through advance purchase commitments, and relegating to second place the international programs that had been designed to achieve a certain level of equity in vaccine distribution.

Experts from different disciplines assert that, to overcome the pandemic, pharmaceutical companies should abandon their exclusive market rights[59,60,61] so that production can be expanded, and the levels of vaccination sufficiently raised to drastically reduce viral transmission, severity of infections, and COVID-19 mortality. From this perspective, in a pandemic, the patents on products that are necessary for improving global health could be violating a fundamental human right. Article 25 of the United Nations Universal Declaration of Human Rights[62] affirms that the right to health is an inalienable human right, recognized also in the WHO constitution[63] and in the constitutions of many countries. Not so many years ago, drugs and vaccines were only protected by process patents, and not in all countries. Today, companies protect their products with multiple patents; some drugs (such as Humira, Enbrel, Keytruda, Revlimid) are protected with more than 100 patents each.

As we have seen, most of the COVID-19 vaccines were developed with public funding, therefore, they should belong to the commons and be patent free, at least for as long as the pandemic lasts. Given the human and economic cost of the pandemic, one would expect that the companies themselves would have waived the patents and set prices close to production costs. In so doing, they would have been fair to the taxpayers and would have contributed to the common good.

The governments of India and South Africa identified the patent problem early in the pandemic and submitted a proposal to be considered at the October 2020 meeting of the WTO. The proposal included waiving patents, technical knowledge, and other non-patented information necessary to produce vaccines and other products on COVID-19 during the pandemic. This would facilitate the production of the necessary vaccine doses and drugs in different countries around the world, allowing for the immunization of the globe in a much quicker manner and the reduction of mortality and the length of hospital stays.

The WTO, the IMF and the World Customs Organization (WCO) were in favor of restricting trade barriers,[64,65] as they were concerned about the impact of the pandemic on international trade and countries' economies, but did not mention the idea of breaking patents. On the other hand, many countries and civil society representatives supported the proposal from India and South Africa.[66] However, when discussing the issue during the WTO meeting in October 2020, the US, Canada, the European Union, the UK, Switzerland, Japan and Australia, countries that manufacture patent-protected products, including medicines, voted against it. There were exceptions. Highly industrialized China, Korea and Russia did not oppose

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it, but abstained from voting, and Brazil, an economic powerhouse based on agriculture, voted against. Since decisions at the WTO are usually reached by consensus, the motion spearheaded by India and South Africa failed.

Following the change in the US government (January 2021), the Biden administration supported the proposal in early May 2021,[67] but only for vaccines and not for the therapies and other technologies needed to respond to the pandemic.[68] The US support encouraged a number of countries to align with the initiative, however, it has not translated into any concrete steps. At the time of this writing, there are speculations that the outcome will offer a solution that is too late to be implemented and does not satisfy the needs of many nations.

After the US changed its position, all attention was focused on how the European Union would respond to the conflict. Although the European Parliament voted in favor of the waiver,[69] the European Commission maintained its initial position. As stated by its President Ursula von der Leyen in May 2021: "An exemption from intellectual property rights will not bring even one more dose of vaccine in the medium and short term" and, as an alternative, she suggested to increase the export of vaccines to other regions of the world.[70]

During the patent discussions, it was stated that the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) includes flexibilities that allow for the issuing of compulsory licenses and public use of inventions for non-commercial purposes. It is true that this agreement can be used to protect public health in certain emergency situations, but due to the complexity of the process, the fear of sanctions, and the trade and political pressures from the US, low- and middle-income have rarely used it.[71] The Office of the United States Trade Representative (USTR) annually prepares the "Special 301 Report," a kind of "blacklist" that includes countries that are not considered to sufficiently protect intellectual property (IP) rights and suggests possible retaliation for the "delinquent" country.

In October 2021, Brussels proposed the discussion of a draft proposal that reiterated the safeguards included in TRIPS and mentioned in the 20 year-old Doha Declaration. This alternative has been heavily criticized by experts, who argue that it focuses only on products, and avoids mentioning underlying technologies, components, raw materials, processes, and methods whose intellectual property is protected and are equally important for the companies interested in manufacturing the final product.[72] In addition, as mentioned, most products are protected by several patents, and each country must issue compulsory licenses for each one of them, which is time-consuming and does not allow for the desired rapid response in a pandemic.

The use of compulsory licenses without a broader global patents' exemption framework could take years. According to one expert, the alternative proposed by the European Union is "a delaying tactic that is not designed to solve the problem but to obstruct any workable resolution."[73] The case of the Biolyse, a Canadian pharmaceutical company is a good example.[74] One of Biolyse's objectives is to market low-priced pharmaceuticals in the Canadian market and in developing countries. Biolyse has the capacity to manufacture up to 20 million doses of COVID-19 vaccines per year.[75] In May 2021, the government of Bolivia and Biolyse signed an agreement by which Bolivia would receive 15 million doses of COVID-19 vaccines. At the time only 5% of the Bolivian population had been vaccinated. Biolyse's vaccines would have sufficed to vaccinate most of the remaining 8.5 million unvaccinated adults. However, the agreement could not be implemented due to unwillingness of the Canadian government to issue a compulsory license. The government's decision is in clear contradiction with the Canadian declarations before the World Trade Organization. As of April of 2022, it is estimated that 57% of the Bolivian population has been vaccinated, and 21,906 COVID-19 deaths have been reported.[76]

Patents allow companies to make disproportionate profits. In 2021, Pfizer earned

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US$36.8 billion from COVID-19 vaccine sales,[77] and in 2022 expects to make US$32 billion.[78] These revenues have been achieved by selling to middle-income countries at half price and at production cost to low-income countries. Vaccine sales account for 60% of the company's revenues.[79] For 2022, Pfizer expects $54 billion in sales on COVID-19 vaccine and treatment pill.[78] Albert Bourla, Pfizer's CEO, received a total compensation of US$24.3 million in 2021, a 15% increase over the previous year.[80] Pfizer shares started 2021 at US$37 per share and after peaking at US$61, ended the year at US$58.

Baker and Silver[81] explain how Pfizer has managed to avoid the breaking of its vaccine patents through vaccine donations and price reductions, and the fear generated within the company by the possibility of the Biden's administration deciding to support the patent waiver. For example, in November 2021 Pfizer released its vaccine profits and announced that it would provide one billion doses of to the US government, at a not-for-profit price, for distribution to developing countries anywhere in the world.[82]

This action can be interpreted as an attempt to change the negative image that the population was beginning to have of the company, due to its excessive profits. On the other hand, organizing the distribution of one billion vaccines to developing countries is costly, and the company has transferred that cost to the US government. It can also be interpreted as a lobbying strategy to avoid a decision at the international level to temporarily suspend patents, or to prevent the US Congress from passing a law controlling drug prices in the US. Providing vaccines at cost is a smart decision. Lost profits are tax deductible. The donation of a billion vaccines will provide Pfizer with a "billionaire deduction" and an image of generosity. In fact, through its generous act, the company could make a profit.

During the pandemic, AstraZeneca, which marketed the vaccine developed by Oxford University with funding from the UK government, had to keep prices low (close to the cost of production). As a result, its profits have been considerably lower than those of Pfizer or Moderna, but not negligible, around one billion dollars. As the contract with Oxford University did not establish who would determine the end of the pandemic, AstraZeneca declared that as of November 2021 it could start raising the vaccine prices, although according to the Oxford contract low-income countries will continue to buy them at production cost.[83] AstraZeneca's CEO Pascal Soriot received a total compensation of US$18.76 million in 2021, down from the US$21.52 million he received in 2020.[84] At the beginning of 2021, a share of AstraZeneca was worth US$50, peaked at US$64 and closed the year at US$58.

The case of Moderna is more scandalous, because apart from being the company that has received the most public resources, its vaccine price is the highest. Moderna was created in 2010, and in 2020 it had not brought any product to market. In 2020, 60% of its revenues came from grants, 35% from sales (advanced commitments), and 5% from collaborations. Lacking sufficient production capacity, it was unable to respond to the pandemic as could have been expected from a company that received so much economic and scientific support.[85] Now, all their sales are practically limited to COVID-19 vaccines.[85] In 2020, the company had losses of US$233 million, but thanks its COVID-19 vaccine, by September 30, 2021, it had posted profits of US$7.3 billion.[86] Moderna's CEO Stephane Bancel's compensation in 2021 reached US$18.2 million, up 41% from the previous year,[87] and the company's stock that started 2021 at US$111 per share, in August had peaked to US$484 and ended the year at US$252.

The price of Moderna, Pfizer, and Johnson & Johnson vaccines creates problems for low- and middle-income countries. The resources used to purchase the vaccines come from other public programs, including those of the Ministry of Health. If current prices are maintained, low- and some middle-income countries may have a hard time vaccinating most of their population.

As is the norm for innovative pharmaceutical companies, the prices of their products

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do not correspond to production and development costs; they are based on what they believe buyers are willing to pay. Munira et al.[88] calculated the average cost of producing 12 vaccines in eight developing countries, and documented that in 2018, the average cost of producing one dose of vaccine was US$2.18 with a range from US$0.98 to a maximum of US$4.85. The cost of producing a dose of vaccine for COVID-19 has been calculated to be US$1.28, which explains the large profits that the pandemic has represented for companies and their investors,[89] and the advantages of producing COVID-19 vaccines in low- and middle-income countries.

As of April 14, 2022, the decision on whether WTO approves the proposal by India and South Africa and exempts some (like vaccines), all, or none of the COVID-19 products from the obligations acquired when signing the TRIPS agreement is still pending. This issue should have been resolved during the 12th WTO Ministerial Conference (November 30-December 3, 2021), was postponed until March 2022 for unclear reasons, but it is yet to happen; observers expect it be discussed at a formal WTO meeting very soon.

With the crisis generated by the war in Ukraine, political attention to the pandemic is already waning, not only at the WTO. The producers of vaccines point to overproduction of vaccines, which is further complicated by other factors, such as vaccine hesitancy and logistical problems in immunizing people especially in low- and middle-income countries. However, given that nearly three billion people remain unvaccinated against COVID-19 and that the need for therapies and diagnostics has not diminished, the relevance of the TRIPS waiver remains important, not only for the present pandemic but for future ones.

Given the level of profits that patent-protected vaccines represent for companies, it should come as no surprise that pharmaceutical companies continue to claim that:

> The waiver proposal is based on the incorrect notion [...] lifting IP restrictions won't help vaccinate people more quickly [...] The industry is already well on its way to produce enough vaccines for the entire world by the middle of next year [2022].[81]

In fact, Thomas Cueni, Director General of the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) said during a media briefing on April 13, 2022:

> I am stunned that the proposed IP waiver is still being debated while supplies of vaccines are far outstripping demand and some factories have been put to a halt because of missing orders [...] Now orders are slowing down. Countries as well as organizations such as Africa CDC, are not only asking for orders to be delayed but are cancelling them [...] Leading voices are still calling out vaccine scarcity. I do understand the concern. Vaccines are not reaching all those who need them. But the cause is no longer the lack of supplies. It's scarcity of vaccination, which is due to the lack of country readiness, absorption capacity and the lack of resources needed to get the vaccines into arms.[90]

This statement was echoed by Pfizer's CEO Albert Bourla: "The problem is not if there is availability or access to pricing. The problem is that the infrastructure of these countries is very poor, so they cannot absorb them. They cannot run a vaccination campaign," and he added that what has been learned from this pandemic is the need for governments to prepare countries to vaccinate.[90] It could be added that it has also been learned that it is necessary to have vaccine manufacturing capacity in several locations, including low- and middle-income countries, and to have corporations be willing to waive their patents.

The fear that, for the first time since the signing of the TRIPS Agreement in 1994, pharmaceutical patents might be waived led Eli Lilly's CEO, David Ricks, to make questionable

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allegations: pharmaceutical companies and investors would "never have invested" in the development of COVID-19 vaccines "if there was not the promise of IP."[90] History has shown that this is not the case. During previous decades pharmaceutical products were not patented in many places in the world but were still being developed and sold.

One year and a half after the vaccines were developed with financial and scientific assistance from governments, it is easy to transfer the failure of controlling the pandemic to governments. It is well understood that vaccines are necessary but not sufficient to end a pandemic. Whatever might have been the failures of governments and other parties, it is ethically difficult to accept that these companies, aware that they could not manufacture the vaccines in a timely manner were unwilling to waive their patents. The only explanation is the desire of gaining billions of dollars at the expense of illness and death.

The fact is that nearly three billion people remain unvaccinated against COVID-19 and that the need for therapies and diagnostics has not diminished; the relevance of the TRIPS waiver remains important, not only for the present pandemic but for future ones.

CONCLUSION

It can be stated that the plans that were developed to vaccinate the world have failed. The reasons for the failure are multiple and should be analyzed in detail to avoid the same mistakes in future pandemics. What has been presented in this article tells us that:

1) The process of researching and developing effective vaccines can be accelerated.
2) The capacity to produce vaccines is not exclusive to the multinational pharmaceutical industry; relatively small research groups (such as the case of the vaccine developed in Texas), and low and middle-income countries are also capable of producing effective vaccines.
3) Governments in high-income countries have invested large amounts of money in stimulating the development and production of vaccines by the private sector, without imposing any conditions on the recipients of those resources. As a result, taxpayers have paid for the R&D of most vaccines, as well as for the doses that have been administered. It is important to discuss fair forms of financing the R&D of vaccines and other treatments, as well as the price of the finish products, to prevent the use of the public purse for generating large profits for companies, their CEOs and investors.
4) It was known from the beginning that the installed capacity to produce vaccines was insufficient to supply the world market, and even knowing that the safety of the world depended on vaccinating everyone, multinational companies refused to share their intellectual property to allow vaccine producers from around the world to manufacture COVID-19 vaccines.
5) Pharmaceutical companies that produced vaccines prioritized profit over global safety.
6) Governments of high-income countries chose to protect the interests of companies located in their territory, and to vaccinate their residents, knowing that this would not end the pandemic.
7) Voluntary mechanisms of global cooperation have failed. To protect the world's population in the next pandemic, binding mechanisms will have to be established now, as soon as possible.
8) The citizens of the world lent their bodies to contribute to science and to the development of vaccines, but their efforts were not adequately recognized by either companies or governments. Companies imposed excessive prices on vaccines, preventing universal access, and failed to adequately plan for unblinding research participants when the first COVID-19 vaccines were approved for emergency use. Governments did not develop adequate pharmacovigilance plans that would make it possible to know the safety and efficacy pattern of new vaccines.

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9) Perhaps more needs to be invested in strengthening public research centers to ensure that in future pandemics governments are more willing to share the intellectual property of their inventions with other stakeholders to better protect their populations and contribute to the common good.

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