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Production of COVID-19 vaccines in Brazil: major challenges in production and distribution capacity in a post-pandemic world

Danilo Jorge Vasconcelos Silva[1]*; Sérgio Barros Silva[2]; Lais Marília Souza do Nascimento[3]; Jorge Wilian dos Santos Silva[4]; Ana Tassia de Arruda Dutra[5]; Eduarda de Souza Silva[6]; Elivelton Davino Manuel Ferreira[7]; Oséias Calebe Vidal de Negreiros[8]; Jaise Braz Cabral[9]; Sabrina Rafaela Nery dos Santos Ribeiro[10]; Tarcísio José Moura Aguiar[11]; José Wilian Pereira Barbosa[12]; Vitória Maria Muniz Ferreira[13]

1 - 13 Bachelor of Pharmaceutical Sciences from the University Center of Vitória de Santo Antão -UNIVISA

E-mail adresse: Danilo Jorge Vasconcelos Silva (danilojorge39@gmail.com)
*Corresponding author

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Abstract: In a country like Brazil, with continental dimensions and a population of 215 million inhabitants, protecting so many people and eradicating or controlling diseases is a huge challenge. After the approval of the first coronavirus vaccine by the National Health Surveillance Agency (ANVISA) 549 million doses were distributed to all federative units. Proper communication with the population, informing the real benefits of the vaccine, its limitations and the importance of individual and collective protection is still a great challenge to be faced and trust in vaccines needs to be maintained at any cost, under penalty of putting at risk all achievements achieved in control and elimination and diseases worldwide. Strong coordination must be established between researchers, regulators, policymakers, funders, public health agencies and government, in order to ensure that vaccines continue to be opened in our country and provided to the entire population.

Keywords: Vaccination. COVID-19. Public Health. Production.

1. Introduction

The genetic sequence of the COVID-19 virus triggered intense global research activity to develop a vaccine against the disease and this has boosted the use of new vaccine technology platforms to accelerate research (Lurie *et al*, 2020). The reduction of the process to a period of 12 to 18 months involved about 175 research teams worldwide, updated by the World Health Organization (WHO), with projects from public and private sources.

Several production technologies such as nucleic acids, use of viral vectors, viral vaccines and protein vaccines were used (Mukherjee, 2020) and some of these platforms had never been used in vaccines already licensed (Thanh *et al*, 2020). Most of the vaccines studied for COVID-19 aimed to induce neutralizing antibodies against viral subunits, most of them targeting the RBD region of the virus's most conserved protein, Spike (S), thus preventing the capture of the virus by the human ACE2 receptor (angiotensin-pulse 2-converter enzyme) (Caddy, 2020).

The Vector-based ChAdOx1 nCoV-19 vaccine, developed at the University of Oxford in England in partnership with the AstraZeneca laboratory, induced a robust immune response, including cellular response, after two doses were applied. The U.S. lab Johnson & Johnson also tested a vaccine based on viral vectors. The results of the phase 1 and

2 tests were encouraging and phase 3 trials began in August on a global scale, including research center in Brazil (Mercado *et al*, 2020)

Other vaccines based on viral vectors have been released for restricted use in certain population groups in China and Russia (Zhu *et al*, 2020).

Also, with the technology of the use of adenovirus, began vaccination of health professionals and teachers with vaccine produced by the Gamaleya Institute in Moscow and the government of the state of Paraná negotiated access to the so-called Sputnik V vaccine.

Genetic vaccines of messenger RNA have demonstrated an excellent safety profile and good cellular and humoral immune responses. being produced on a larger scale, because they are synthetic products, and the disadvantage of being products that require freezing conservation (Krammer, 2020).

The American Modern Laboratory, in partnership with the National Institute of American Health (NIH), began clinical testing of its messenger RNA-based vaccine (mRNA-1273) just two months after the virus sequence was identified and published its study of human volunteers. The vaccine, which encoded stabilized S protein, resulted in the production of a large number of neutralizing antibodies in all participants studied, detected by two different methods, and with values similar to those of serum samples from convalescent patients, with self-limited adverse events (Jackson *et al*, 2020).

Also based on mRNA, the vaccine produced by the American laboratory Pfizer, in partnership with the German biotechnology company BioNTech, demonstrated good response in the induction of humoral and cellular immunity in their studies and the results showed titers of neutralizing antibodies on average 1.8 to 2.8 times higher when compared with covid-19 convalescent human serum panel. 17 The study had about 30,000 participants in countries such as Brazil, Argentina and Germany, in addition to the United States (Logunov *et al*, 2020).

Viral vaccines such as that of the Chinese laboratory Sinovac used the classic inactivated virus platform, with cell culture of the virus in very cells with subsequent inactivation. In Brazil, it has established a partnership with the government of the State of São Paulo, through the Butantan Institute, and is being produced in Brazil on a large scale (Sharpe *et al*, 2020).

Protein vaccines such as the Novavax laboratory used a recombinant version of the S protein developed with nanoparticle technology, associated with an adjuvant, and the results demonstrated safety and immunogenicity (Folegatti *et al*, 2020).

In an unprecedented collaboration, two of the world's largest vaccine producers, Sanofi Pasteur (France) and GlaxoSmithKline laboratories (GSK-UK), joined forces and produced a protein vaccine (Grifoni *et al*, 2020).

2. Methodology

This is a study with data collection based on bibliographic data collection. For this survey, articles were retrieved in several databases such as The Clinical Contexts (PepsiCo) and SciELO Brazil. The inclusion criteria determined for the selection of articles were: texts available in full, articles in Portuguese and In English from 2019 to 2022; master's dissertations and doctoral theses and articles in full that portray the Importance of vaccines for individual and public health. All opinions or unreferenced texts served as exclusion criteria in this study.

3. Results and Discussion

The viruses challenged vaccine manufacturers, rapidly changing so that antibodies acting on one viral strain failed in another and the new coronavirus was no different and a vaccine that could be considered effective should work in any country (Dearlove *et al*, 2020).

The World Health Organization (WHO) made a proposal to the European Union recommending a voluntary patent pool, which would pressure companies to give up their monopolies on the vaccines they have developed (Natalie, 2020) and a WHO initiative in partnership with the GAVI Global Vaccine Alliance - COVAX, has brought countries together in a fund to make vaccines available equally among all countries that sign the agreement. Oxfam, an international charity, published an open letter to 140 world leaders and experts calling for a "people's vaccine," and made available free of charge to all people in all countries, and Helen Clark, former Prime Minister of New Zealand, who also signed the letter, commented that "vaccines against COVID-19 needed to be a public good and that no one sure everyone would be not (Amanat and Krammer, 2020).

Just over half of the candidate vaccines were developed by private companies, while about 45% of the projects were led by universities, the public sector and other non-profit organizations (Thanh *et al*, 2020).

Today, more than 33 countries are developing research for the production of vaccines against SARS-CoV-2 (FDA, 2020) and in Brazil, where the Federal Government, through the Ministry of Health, has not implemented an articulated and coordinated national action to control the pandemic, the number of cases followed among the highest in the world. Still, the country is among those participating in international studies and began the production of two vaccines, resulting from multicentric research (Sinovac; Butantan, 2022)

One of them, developed in cooperation between the pharmaceutical company AstraZeneca and the University of Oxford (United Kingdom), had the partnership of the Federal University of São Paulo (Unifesp) and was manufactured in the country by the laboratory Bio-Manguinhos, Fiocruz (Radio Bandeirantes, 2020).

The other, developed by Chinese bio-pharmaceutical Company Sinovac BioNTech, is in full production at the Butantan Institute. For the development of vaccines against Covid-19, a multicenter and multisectoral effort allowed channeling intense international investments aimed at research

and production of immunizations in the face of the disease.
In the race for an efficient and safe vaccine against Covid-19, the use of several candidate vaccines using different platforms increased the chances of good immunization results, and although some technologies were new, all proved promising.
Among the challenges faced was production capacity and equitable distribution between countries. According to an article published in the journal Nature in August, the global production capacity of the different vaccines, in the authorization phase and beginning of application, would reach something close to 11 billion doses by the end of 2021.

Through Covax, 92 poor countries had access to 1.3 billion doses of some Covid-19 vaccine in the first half of 2021 and 80 other countries, including Brazil, appear on covax's list as economies with "potential self-financing".

However, the country had bilateral access strategies, such as the transfer of technology from AstraZeneca to Fiocruz, with the possibility of production in Bio-Manguinhos of approximately 220 million doses in 2021, and from Sinovac BioNTech to the Butantan Institute, with the production possibility of 100 million doses by the end of the first half of 2021.

4. Conclusions

Currently, the National Health Surveillance Agency (Anvisa) has approved the use of the covid-19 vaccine in children aged between 6 months and 4 years of life in Brazil. The endorsement, granted on Friday (16), was aimed specifically at the immunizing Pfizer, which until then had only authorized use in children over 5 years in the country.

Pfizer has been authorized in the country since February 2021. To release the use of the product in the new age group, the municipality considered not only clinical data that prove the safety and efficacy of the vaccine in the public of this age group, but also the evaluation of a series of experts from the Brazilian Association of Collective Health (Abrasco), of the Brazilian Society of Pulmonology and Tisiology (SBPT), of the Brazilian Society of Infectious Diseases (SBI), The Brazilian Society of Immunology (SBI) and the Brazilian Society of Pediatrics (SBP). The vaccination schedule of the new public to be vaccinated should be organized by the Ministry of Health (MH) and immunization should follow procedures different from those adopted in the rest of the population.

However, the public's willingness to support measures to use masks to reduce the spread of COVID-19, for example , is still deficient in Brazil and the success in controlling the pandemic, in a way that is, depends on a set of combined actions and a guarantee of financing that will segregate the government, private initiative, vaccine manufacturers and the people themselves, for an integrated awareness, seeking an outcome where there is protection for all. Only this joint effort will extinguish the pandemic in our country.

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