**COVID-19 VACCINES: BIOETHICAL CONSIDERATION**

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**ABSTRACT:**

The COVID-19 pandemic generated immeasurable impacts on the economy, education, socialization and the loss of millions of lives. Thus, there has been an acceleration in the development of an unprecedented number of COVID-19 vaccine candidates to control the pandemic. In turn, the implementation of the authorization for emergency use by the World Health Organization allowed the start of immunization of the population through COVID-19 vaccines, which are still clinical trials. Herein, we present a perspective of the bioethical precepts of autonomy, non-maleficence, beneficence and justice in the context of the emergency use of COVID-19 vaccines. Furthermore, the importance of surveillance at all stages of vaccine development in order to detect adverse effects and ensure compliance with bioethical precepts is emphasized.

**KEYWORDS:** COVID-19; Vaccines; Bioethical, World Health Organization; Immunization; Adverse effects.

**RESUMEN**

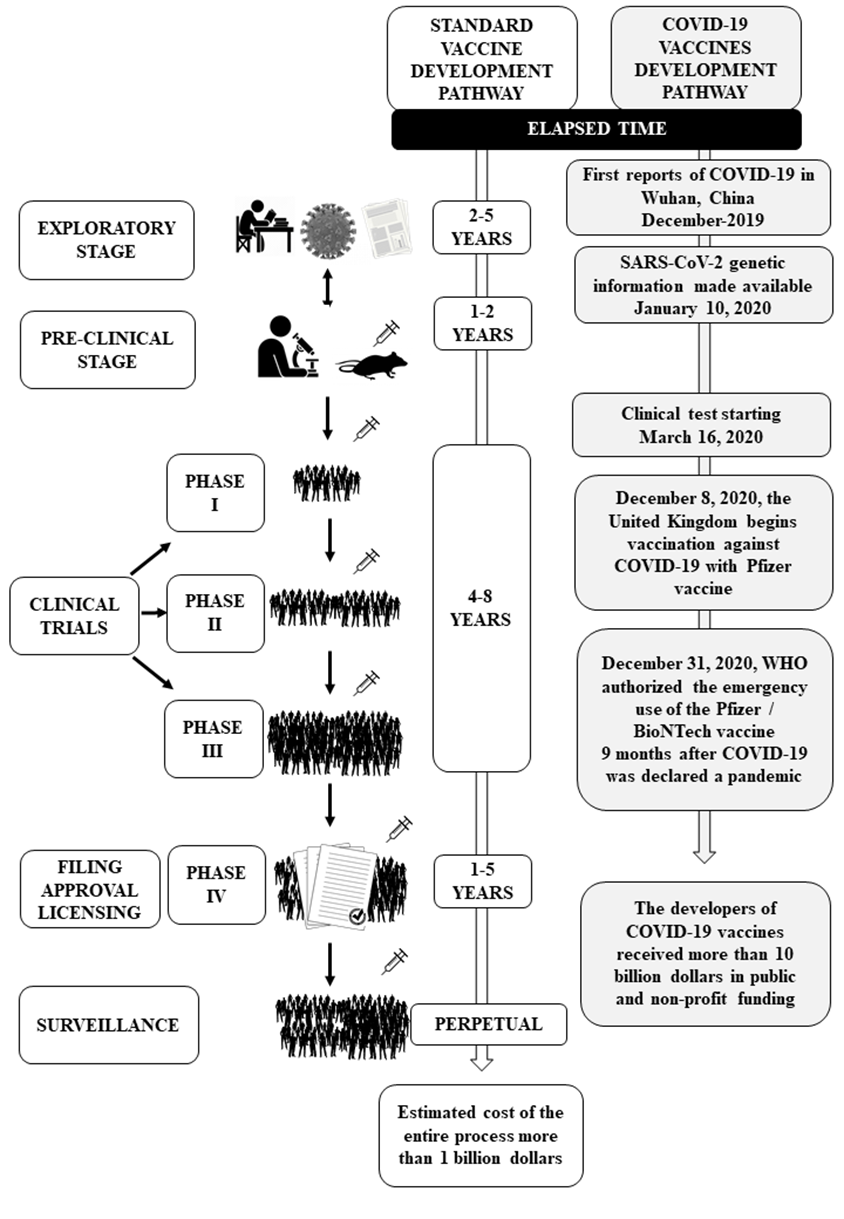
La pandemia de COVID-19 ha tenido impactos inconmensurables en la economía, la educación, la socialización y la pérdida de millones de vidas. Por lo tanto, se ha acelerado el desarrollo de un número sin precedentes de candidatos a vacunas COVID-19 para controlar la pandemia. A su vez, la implementación de la autorización para uso de emergencia por parte de la Organización Mundial de la Salud permitió el inicio de la inmunización de la población a través de las vacunas COVID-19, las cuales aún se encuentran en ensayos clínicos. Aquí presentamos una perspectiva de los preceptos bioéticos de autonomía, no maleficencia, beneficencia y justicia en el contexto del uso de emergencia de vacunas contra COVID-19. Además, enfatiza la importancia de la vigilancia en todas las etapas del desarrollo de la vacuna, con el fin de detectar efectos adversos y asegurar el cumplimiento de los preceptos bioéticos.

**PALABRAS- CLAVE:** COVID-19; Vacunas; Bioética; Organización Mundial de la Salud; Inmunización; Efectos Adversos.

**1 INTRODUCTION**

The impacts of the COVID-19 pandemic, whether on the economy, education, socialization and, mainly, that represented by the loss of millions of lives, are immeasurable (1–3) Thus, in order to contain the spread of the virus, measures such as the use of facemasks by the population, social distancing, use of tests for tracking patients and even lockdowns have been implemented in different parts of the world. Furthermore, a race was started to develop drugs for the treatment of patients with COVID-19 and, above all, vaccines that can interrupt viral transmission through collective immunity, avoid the occurrence of moderate to severe forms of the disease, reducing morbimortality.(3–7)

In fact, vaccines have unquestionable value in health promotion and disease prevention.(5,8) However, vaccines development is a process characterized by both low public investment and a 10 to 30-year long process for pre-clinical stages, clinical tests, until it reaches large-scale production after approval and licensing..(2,3,7,9) In contrast, the development of COVID-19 vaccines has been characterized by great public funding, a speed and number of candidates for COVID-19 vaccines, until then, unimaginable. (3,8) Thus, a comparison of the time flow, steps and investment required for traditional vaccine development versus the current flow of vaccines against COVID-19 is shown in Figure 1.(2,7,10–12)



**Figure 1. Comparison between the pathway of traditional vaccine development versus the pathway of COVID-19 vaccines.**

Figure 1, shows that there was an acceleration in the process of developing vaccines against COVID-19 with a shortening of the time of up to 20 years to reach vaccination in a commercial model to about 9 months for the first person in the world to be vaccinated against COVID-19 in the United Kingdom, although its stage of development was still clinical trials.(2,7,10,11,13,14) It is noteworthy that the traditional vaccine development process is characterized by stages that have well-defined objectives, as shown in Table 1.(2,10–12)

**Table 1. Steps and respective objectives of the traditional vaccine development process**

|  |  |  |
| --- | --- | --- |
| **Vaccine development stage** | **Objectives** | |
| Exploratory | To study pathology both from the viewpoint of biological structure, genetic sequencing of the pathogen and its pathogenic mechanism, as well as the course and clinical characteristics including possible drugs with some therapeutic action and epidemiology.  Identify possible antigens. | |
| Pre-clinical | Assess the capacity to induce an immune response (immunogenicity) and safety, through the use of cell culture and animal tests.  Assess the appropriate route of administration, adjust the dose and determine "Good Manufacturing Practices" for the production of the batches for the phase II tests.  Characterize the antigen and assess toxicity.  Investigate cellular response and possible mechanisms of immunity. | |
| Clinical Trials | Phase I | Assess in a small group of adult individuals: safety, dosage variations and immunogenicity, including the extent and type of the immune response. |
| Phase II | Assess in a group of hundreds of individuals, which, may include individuals from risk group to acquire the pathology: immunogenicity, safety, with variation in dosage, efficacy and variations in the immunization schedule. |
| Phase III | Assess in a large group of individuals, preferably in a multicenter study: immunogenicity, efficacy and safety, mainly regarding rare adverse events. |
| Filing, Approval and Licensing | If preliminary tests are successful, the vaccine manufacturer will apply for a license from the regulatory health agency, which will inspect the manufacturing facilities.  Assess the cost-benefit of the immunizer and its possibility of implementation.  If the licensing is approved, the manufacturer continues to undergo inspections, test reviews and analyzes of vaccine batches by health regulatory agencies periodically, which may include Phase IV tests. (Pharmacovigilance Measures) | |
| Phase IV | Monitoring of safety, efficacy and other possibilities of use, incorporating pharmacovigilance measures. |
| Surveillance | Assess, notify, monitor and implement a database regarding the occurrence of adverse events in the use of vaccines. | |

In this context,, the acceleration in the development process of COVID-19 vaccines, which, has allowed the rapid implementation of immunization plans, can be explained in part by the huge investment of public and non-profit institutions in companies with candidate vaccines and in the employment of emergency authorization use, such as that issued by the World Health Organization (WHO).(3,4) Thus, in November 2021, 20 months after the WHO characterized COVID-19 as a pandemic, situation for the development of COVID-19 vaccines was:: 329 vaccine candidates, of which 111 were in clinical testing, 23 in use and 7 vaccines had already received WHO emergency authorization use, which , are still undergoing clinical trials. (10,11,15) Furthermore, it is clear that in addition to WHO, countries also have the autonomy to issue an emergency authorization use for vaccines internally in their domains regardless of whether or not they are authorized by WHO, consequently, the number of vaccines currently in use in the world is greater than the number of vaccines with emergency use authorization issued by WHO.(10,15)

**2 EMERGENCY USE AUTHORIZATION IN PUBLIC HEALTH**

An emergency use authorization can be defined as an action by a health policy regulatory agency whether national, group of countries or worldwide, which aims to allow the employment of unapproved medical products, including vaccines, during public health emergencies.(8,16) However, for an emergency use authorization to be deliberate, it is necessary that for a given public health emergency, there are no other suitable and safe alternatives, be it diagnosis or treatment, which. are already available and approved by the public health regulatory agency.(8,16) Once these requirements are met, it is still necessary for the company interested in making the health product available for emergency use, submit it to the regulatory agency for health policies.(8,16) Subsequently, the regulatory agency may, according to its internal requirements, determine whether the health product can be approved for emergency use or not.(8,16)

Similarly, the entire context mentioned above applies to an emergency authorization of COVID-19 vaccines, since the COVID-19 pandemic is configured as a public health emergency, where there is no approved and adequate health product for its prevention and treatment.

Thus, the WHO emergency use authorization for COVID-19 vaccines is a risk-based procedure that assesses vaccine candidates in order to allow both United Nations agencies responsible for purchasing vaccines and their member countries to purchase vaccines, which were previously approved by WHO on criteria related to safety, quality, performance and efficacy.(17,18) Furthermore, the manufacturers of COVID-19 vaccines are under constant surveillance to commit themselves to standards of excellence in the manufacture and distribution of vaccines.(17,19) Thus, the main objective of WHO emergency use authorization for COVID-19 vaccines is to accelerate the availability of vaccines for immediate use in immunization plans.(18) In this sense, Table 2 presents the eligibility criteria, analyzed aspects and, post-authorization guidelines that a vaccine candidate must comply with until obtaining its emergency use authorization from WHO.(17,18)

**Table 2. Eligibility criteria, assessed aspects and post-authorization guidelines in the WHO emergency use authorization for COVID-19 vaccines**

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| --- | --- |
| Eligibility criteria for WHO emergency use authorization for COVID-19 vaccines | * Emergency use authorization applies to cases in which there is a serious illness, which implies an immediate risk of life. * The disease must have the potential to cause an outbreak, epidemic or pandemic, with no licensed products for indication or, existing vaccines and drugs were unable to eradicate the disease or prevent outbreaks. * The vaccine must be manufactured in accordance with the guidelines for current Good Manufacturing Practices. * The requesting company must commit to completing product development and require prequalification by WHO as soon as the vaccine is licensed. |
| Aspects assessed by WHO | * As vaccines are still in development (unlicensed) WHO will assess in a risk-benefit analysis: quality, safety and efficacy (or performance) using data generated during development to decide whether such vaccines can be used outside clinical trials. * For a candidate for COVID-19 vaccine to have its emergency use approved, it must prove through consistent data that there is a benefit to the target population greater than the risks. |
| Guidelines after WHO emergency use authorization for COVID-19 vaccines | * If a vaccine is approved by a WHO signatory nation, there will be no duplicate evaluation, but WHO will evaluate that vaccine for quality, safety, efficacy and performance criteria. * Authorization for emergency use only aims to make vaccines immediately available to the population. Thus, as vaccines are still in the clinical testing phase, manufacturers are required to continue the traditional process of vaccine development until, eventually, if all previous steps are successful, they reach definitive licensing. * It is mandatory that the companies that develop COVID-19 vaccines present a risk management plan and appropriate guidelines for the population. * The surveillance of COVID-19 vaccines will be permanent. |

Therefore, based on the aspects referred to in Tables 1 and 2, the authorization process for emergency use of COVID-19 vaccines, in practical lines, can be accelerated through cooperation between international health agencies and these with WHO, avoiding multiple duplicate analyzes and with the planning and realization of the phase II and III tests even before the phase I tests are finished and, preferably, simultaneously in several countries.(2,6,7,10–12,17,18) Thus, the benefit in a pandemic crisis of obtaining vaccines in a short time is undeniable. However, starting the distribution and immunization of the population with vaccines in the stage of development of clinical tests through authorization for emergency use requires special ethical attention and permanent surveillance in every process, whether in the pre-clinical and clinical testing phases as well as after the future licensing. In this sense, Figure 2 highlights the importance of surveillance in the development process and availability for immediate use of COVID-19 vaccines through authorization for emergency use.



**Figure 2. Diagram representing the importance of surveillance in the process of development and availability for immediate use of COVID-19 vaccines through emergency use authorization.**

Note that in Figure 2, it is proposed that surveillance ceases to be characterized as the last stage in the vaccine development process as shown in Figure 1 and becomes one of the fundamental requirements of pre-clinical and clinical tests so that, effectively, ethics requirements are met.

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**3 BIOETHICS APPLIED TO THE EMERGENCY USE OF COVID-19 VACCINES**

Once exposed that the pandemic situation requires efforts for the rapid implantation of immunization programs, a new ethical discussion is established as the authorization for emergency use implies using vaccines in a situation where:

* In the exploratory stage, many questions remain open regarding the pathogenic mechanism of SARS-CoV-2, variations in clinical courses presented by patients and, mainly due to the appearance of new strains.(6,20)
* The selection of an ideal animal model that reproduces the clinical disease in an evident way, to study the pathogenesis of SARS-CoV-2 could require long-term studies.(2) Thus, in contrast, to the gold standard considered for a vaccine, which is defined as the prevention of infection, studies in primates have shown results that indicate a reduction in viral load and a lower risk of evolution of the patient to severe forms of COVID-19.(6) In addition, the choice of an animal model that does not allow a direct correlation with humans can create impediments about obtaining approval from the ethics committee for research on animals since there would be no glimpse of beneficence in the infection of animals in favour of science.
* Vaccine tests in phases I and II generally involve adults, without comorbidities, which, according to current evidence, would not be an ideal representative group for the population at greatest risk of morbimortality for COVID-19. Likewise, questions regarding adverse reactions, durability and type of immune response may not be sufficiently answered even in phase III studies, if the time factor is reduced. In addition, the wide availability of candidates for COVID-19 vaccine arriving in clinical trials, implies the concomitance of population immunization cycles and phase I, II and III tests, which can have an impact on research results.(2,6,10–12)

Preliminarily, before the bioethical approach, there is a need to identify the 2 individuals involved in the vaccine development cycle and immunization plan where, in the traditional pathway, the individual who receives a vaccine still in clinical tests is called volunteer and, therefore, voluntarily decides participate by consent form where the potential risks and benefits of vaccination are clarified, being accompanied by researchers in this process. In turn, in the immunization cycle resulting from the emergency use of COVID-19 vaccines, there are one or more vaccines under clinical tests, which have already been included in the immunization plan of a particular country in a global attempt to contain the pandemic where, population and their individuals will be the recipients of this vaccine. Therefore, it is evident that the vaccine development stage is the same in both cases, that is, the clinical testing phase, but the pandemic context requires ethical reflection, since there is a possibility that a COVID-19 vaccine is or non-mandatory and, it is also necessary to define the level of surveillance necessary for the individual, especially regarding potential late adverse effects, which goes beyond the limits of beneficence and non-maleficence. (5) In addition, it must be considered that in some countries clinical trials of new vaccines, that is, the research modality of a candidate for COVID-19 vaccine, can coexist with a fully functioning vaccination plan employing a vaccine with emergency use authorization. , which particularly tends to increase bioethical complexity.(6)

Therefore, it is essential that the basic principles of bioethics referring to autonomy, beneficence, non-maleficence and justice have their approach foreseen in the pathway for the implementation of a mass immunization of the population supported by authorization of emergency use of vaccines.

**Autonomy in the context of** **emergency use of COVID-19 vaccines**

Utilitarianism, liberalism and communitarianism are three theoretical aspects related to the ethical context of traditional use of the vaccine and, therefore, can be a matter of discussion when there is an emergency use of covid-19 vaccines.(5) Thus, Utilitarianism, is a consequentialist approach, which advocates that vaccination policies and actions be directed in order to achieve the greatest possible impact on general well-being..(5,21) In this context, Utilitarianism, could justify the mandatory vaccination to health professionals where there would be a great social impact, since it would preserve professionals who are at the forefront of the care of COVID-19, in a central position of great risk of contamination. and transmission of SARS-CoV-2, in addition to guaranteeing the service of the population, configuring a greater impact on the community as a whole.(5,6,21,22) However, Bowen and WHO, suggest that a mandatory vaccination for health professionals may be opposed to medical ethical precepts related to autonomy, such as self-determination, which could affect confidence in vaccination..(6,21). In turn, in Liberalism it is the individual who determines the benefit of vaccination to himself, while, in Communitarianism, a community benefit from vaccination would be prioritized.(5) In this sense, Afolabi, considers Liberalism and Communitarianism as unethical postulates intended merely to justify social conduct, whether in the sense of vaccination hesitation without justifiable reason in an individual nature or making vaccination mandatory when immune response and safety still remain incompletely elucidated.(5) Therefore, in a pandemic, with global non-equal distribution of vaccines, deciding on autonomy in the emergency use of COVID-19 based strictly on theories can lead to serious bias, since each theory has fundamentals that, separately, can lead to mandatory measures or not.(5,6,21).

Thus, a moderate approach to autonomy as proposed by WHO, in order to balance community and individual well-being may be appropriate in the context of emergency use of COVID-19 vaccines..(22) In this regard, WHO, has highlighted in its policy brief on May 13, 2021, that it does not support any measures for mandatory vaccination for COVID-19, including specific situations such as international travel and, in particular, does not encourage mandatory systems based on threats or restriction of rights such as working. or studies, which may otherwise undermine vaccine confidence.(22) Nowadays, WHO has advised investment in information campaigns to establish confidence in COVID-19 vaccines and in policies that make vaccination accessible.(22)

Another aspect that can enhance autonomy and remain aligned with the Universal Declaration on Bioethics and Human Rights (UDBHR) published in 2005 (23), in the context of emergency use of COVID-19 vaccines, whether because such vaccines reach the plans of immunization categorized based on the traditional vaccine development pathway in a clinical trial stage, where knowledge about immune response, safety and efficacy is not fully understood, it would be necessary to request consent form, prior to vaccination, freely and based on information about the potential risks and benefits of everyone vaccinated.(6,23) It is noteworthy that Article 6 of the UDBHR, it is clear that any preventive medical intervention, where the vaccine is included, necessarily requires a consent form (23). Furthermore, the consent form, when clarifying the individual about the risks and benefits of vaccination mainly in emergency use, allowing his free choice regarding vaccination, contributes to the respect of human dignity, human rights, fundamental freedoms and autonomy exactly as postulated in Articles 3 (Human dignity and human rights), 4 (Benefit and harm), 5 (Autonomy and individual responsibility), 6 (Consent) of UDBHR (23) Thus, good practices in observing Articles from 3 to 7 of the UDBHR are available from the Mid Essex Clinical Commissioning Group, National Health Service of the United Kingdom (NHS), through different types of consent forms, in language accessible to the entire population. (Table 3).(23–25)

**Table 3. COVID-19 Vaccination Consent Forms: categories, target audience and main characteristics**

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| CONSENT FORM CATEGORIES | TARGET AUDIENCE | MAIN CHARACTERISTICS |
| Consent Forms: Adults able to consent themselves | Consent form for adults able to consent | †, ‡ |
| Consent Forms: Care Homes | Consent form for adults able to consent | †, ‡ |
| Consent form for Care Home resident able to consent | †, ‡ |
| Consent form for the Attorney of a Care Home Resident unable to consent for themselves | †, ‡,§ |
| Consent form for a Relative of a Care Home Resident unable to consent for themselves | †,‡, ¶ |
| Consent Forms: Health and Social Care Workers | Consent form for Frontline social care workers | †, ‡ |
| Consent form for Healthcare workers | †, ‡ |
| Consent form for Social care staff | †, ‡ |
| Consent Forms: Housebound Patients | Consent form for the Attorney of a Housebound patient unable to consent for themselves | †,‡, § |
| Consent form For a Relative of a Housebound patient unable to consent for themselves | †,‡, ¶ |
| Easy-read consent form for adults | Easy-read COVID-19 vaccination consent form for adults who are able to consent. | †, ‡ |

† It presents a direction for the individual to receive detailed information for pregnant, planning pregnancy or breastfeeding, where the informative material suggests that pregnant women have Pfizer / BioNTech or Moderna vaccine, due to studies in these groups in other countries do not show important reactions.

‡ If the option is not to vaccinate, there is an invitation to inform the reason for the hesitation regarding vaccination.

§ Who signs is the Attorney for Health and Welfare responsible for the individual who is unable to consent for themselves.

¶ Who signs is the Relative of a Care Home Resident unable to consent for themselves.

According to Table 3, it is noted that to adequately comply with the precepts of Articles 3 and 6 of the UDBHR, the NHS has prepared a variety of consent forms, including even inclusive language and the possibility of the decision of consenting or not being carried out by an attorney for health and welfare or a relative of individuals unable to consent for themselves, which ensures compliance with Article 7 (Persons without the capacity to consent) of the UDBHR. (22–24) Furthermore, special attention is given to pregnant, planning pregnancy or breastfeeding, since vaccines in their initial testing stages do not address these groups and, therefore, some adverse risks may still be unknown, which ensures compliance with article 8 ( Respect for human vulnerability and personal integrity) of the UDBHR. (4)

In turn, the admission of surveillance is a basic requirement for the emergency use of vaccines since the pre-clinical and clinical testing stages, can contribute to autonomy as it could provide important data regarding potential adverse effects and safety, improving the feeling of confidence of individual and community in vaccines, which could result in increased adherence to the immunization plan and combat vaccine hesitation. In addition, the large availability of vaccine candidates, which have different development platforms, suggests that the identification of an adverse effect on a given vaccine on a given platform would not imply the impossibility of being vaccinated, but it would mean that the individual or a certain group of individuals prone to such adversity should be immunized with another vaccine with a different platform and that has not had such an adverse reaction.

**Non-maleficence** **in the context of emergency use of COVID-19 vaccines**

The COVID-19 pandemic as a global humanitarian crisis involves intricate ethical dilemmas such as reaching a balance between not causing harm or non-maleficence and bringing a benefit to others, or beneficence.(5,6,21,26,27) In this sense, as suggested by both Vashishtha and, Kumar and Law and Lo, in the current stage of emergency use of COVID-19 vaccines, it is not possible to admit that the principle of non-maleficence is fully satisfied, given that, issues such as: adverse effects may be unknown, the large number of COVID-19 vaccines carries the risk of different adverse effects for each vaccine development platform, and messenger RNA-based vaccine platforms have not previously been approved for use in humans.(6,26) Thus, surveillance can play an important role as it can prevent the occurrence of serious or late adverse effects from being neglected to cause damage and, through this monitoring, keep the community informed, generating trust and contributing to the non-hesitation in vaccination..

On the other hand, if it is considered that the rush to buy COVID-19 vaccines that some countries promote may cause an imbalance as other nations have their access to vaccines curtailed, leaving their population under the risks imposed by the pandemic, then a maleficence will be configured.(2,4,5) In this regard, COVID-19 Vaccine Global Access Facility (COVAX) co-led by the Vaccine Alliance (Gavi), the Coalition for Epidemic Preparedness Innovations (CEPI), and the WHO (3,4,28,29) plays an important role as it accelerates the development and production of safe vaccines and proposes a way of equal access to the vaccine for all nations. Therefore, COVAX, by encouraging international cooperation for the development and availability of the vaccine for COVID-19 to all nations, seeks to contemplate the interrelated principles as suggested by the UDBHR of equality; non-discrimination; respect for pluralism; solidarity and cooperation; social responsibility and health; transnational practices and international cooperation (23) At the same time, by supporting research and development of vaccines for COVID-19 that are safe and effective, COVAX contemplates the precepts of Article 4 - Benefit and harm of UDBHR (23), which seeks to maximize the direct and indirect benefits for individuals, any possible damage is minimized.

Therefore, making vaccines equally accessible to all peoples, ensuring access to information and surveillance about adverse risks are measures that can contribute to non-maleficence in the emergency use of COVID-19 vaccines.

**Beneficence in the context of emergency use of COVID-19 vaccines**

Beneficence, in the context of bioethics, implies caring for others. In this way, be it for the guarantee of rights, prevention of risks and damages, or accessibility of others to the vaccine, the meaning will always be a vision focused on the protection of another individual, community or nation.(5,6,21,27) In this sense, like non-maleficence, the equal distribution of vaccines would be fundamental for beneficence, generating a real benefit to others, either by immunity in a local herd or by preventing the spread of SARS-CoV-2 in a global context.(3) However, the initial proposal of COVAX, which would be to preliminarily and equally immunize in all nations, the risk groups, which would correspond to 20% of the population and, subsequently, to advance to other groups cannot be reached, once more, that some countries with high economic power have started direct negotiations with manufacturers in order to increase immunization internally in their countries.(3) Anyway, since, inevitably, this race will lead to high vaccination rates in some countries, even if late, it will favor COVAX with less pressure on manufacturers for vaccine delivery and other COVID-19 vaccines entering the market that eventually obtain approval for use.

Otherwise, one has to consider that the benefit of using a vaccine for COVID-19, in terms of the gold standard, would mean its ability to prevent COVID-19 infection.(6) However, for COVID-19 vaccines, a benefit for emergency use has been admitted based on the criteria of viral load reduction and protection of the individual against the manifestation of severe forms of COVID-19.(6,26) In fact, no COVID-19 vaccine will provide 100% effectiveness, with current studies ranging from just over 50% to 95%, implying that for the greatest benefit there is a need for the already vaccinated population to be informed about the need for maintenance. testing measures, social distance, hand hygiene, facemasks and seeking medical care in case of suspected COVID-19, as there are reports of reinfection.(2,4,6,26)

Again, it is noteworthy that surveillance plays an important role in beneficence since it can over time identify risks of adverse reaction, intervene early in cases that require limiting damage, and keep the population informed through the provision of data, which tends to generate confidence in the vaccine.

**Justice in the context of emergency use of COVID-19 vaccines**

Justice in the bioethical environment implies offering equal opportunities for all, seeking to avoid as much as possible any burden on the parties involved, whether from a personal or social point of view.(5,6,27) Thus, in the emergency use of vaccines for COVID-19, personal justice can be configured when the individual is vaccinated, avoiding a burden on society, either by the spread of the pandemic or by the need to allocate greater resources for treatment in case it evolves to a serious form.(5,27) Otherwise, social justice in the scenario of immunization against COVID-19 can be achieved through awareness campaigns about the importance of vaccination or by making immunization mandatory in order to contain the spread of the SARS-CoV-2. (5,27) However, the adoption of balanced measures between the personal and the social can constitute a good way to encourage immunization and avoid strife, since, even under mandatory conditions, vaccination hesitation can still persist.(5,27) In this context, the hesitation related to COVID-19 vaccines in emergency use has been related to the rapidity that vaccines have gone through the development process reaching use in the population, especially messenger RNA platform vaccines, which have no precedent for approval for use in humans and the emergence of conspiracy theories on social networks fueled by the politicization of vaccines.

Therefore, surveillance, can contribute to justice to measure, by seeking a better allocation of resources, providing greater confidence and adherence to immunization plans against COVID-19, as it ensures the population the existence of government control in monitoring effectiveness and safety of vaccines. In addition, measures to collect information about the reason for hesitation as practiced in the NHS consent form can assist in directing broad awareness campaigns that improve the confidence and adherence of the population to COVID-19 vaccines in emergency use.

**5 CONCLUSIONS**

Herein, we present an approach to the bioethical precepts of autonomy, non-maleficence, beneficence and justice in the context of the emergency use of COVID-19 vaccines. Furthermore, the importance of surveillance is highlighted as a fundamental requirement from the stages of clinical and pre-clinical examinations to post-licensing. In this sense, surveillance contributes to the observance of bioethical precepts, especially with regard to monitoring and adoption of early measures in case of adverse effects during the emergency use of vaccines, playing a role in promoting the trust of population in the plans of immunization. However, the new paradigm in vaccine development determined by COVID-19, characterized by high speed in development, a large number of vaccine candidates, availability of new platforms and, in the possibility of emergency use in order to respond to viral spread around the world, requires an expansion of the debates about the bioethical developments arising from the implementation of the immunization plans against COVID-19.

**REFERENCES**

1. WHO. WHO Coronavirus (COVID-19) Dashboard. WHO Coronavirus (COVID-19) Dashboard With Vaccination Data [Internet]. Who. 2021 [cited 2021 May 14]. p. 1–5. Available from: https://covid19.who.int/

2. Tregoning JS, Brown ES, Cheeseman HM, Flight KE, Higham SL, Lemm N ‐M., et al. Vaccines for COVID-19. Clin Exp Immunol [Internet]. 2020 Nov 18;202(2):162–92. Available from: https://onlinelibrary.wiley.com/doi/10.1111/cei.13517

3. Wouters OJ, Shadlen KC, Salcher-Konrad M, Pollard AJ, Larson HJ, Teerawattananon Y, et al. Challenges in ensuring global access to COVID-19 vaccines: production, affordability, allocation, and deployment. Lancet (London, England) [Internet]. 2021 Mar 13;397(10278):1023–34. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673621003068

4. Flanagan KL, Best E, Crawford NW, Giles M, Koirala A, Macartney K, et al. Progress and Pitfalls in the Quest for Effective SARS-CoV-2 (COVID-19) Vaccines. Front Immunol [Internet]. 2020 Oct 2;11:579250. Available from: https://www.frontiersin.org/article/10.3389/fimmu.2020.579250/full

5. Afolabi MOS. Vaccination. In: Encyclopedia of Global Bioethics [Internet]. Cham: Springer International Publishing; 2016. p. 2911–8. Available from: http://link.springer.com/10.1007/978-3-319-09483-0\_432

6. Vashishtha VM, Kumar P. Emergency use authorisation of Covid-19 vaccines:An ethical conundrum. Indian J Med Ethics [Internet]. 2021 Feb 16;06(01):20–2. Available from: https://ijme.in/articles/emergency-use-authorisation-of-covid-19-vaccines-an-ethical-conundrum/

7. Ospina Henao S, Marín Mora A, Chan Solano F, Ávila-Aguero ML. Bioethical Implications in Vaccine Development, a COVID-19 Challenge. Cureus [Internet]. 2020 Sep 18;12(9):e10530. Available from: http://www.ncbi.nlm.nih.gov/pubmed/33101792

8. Krause PR, Gruber MF. Emergency Use Authorization of Covid Vaccines — Safety and Efficacy Follow-up Considerations. N Engl J Med [Internet]. 2020 Nov 5;383(19):e107. Available from: http://www.nejm.org/doi/10.1056/NEJMp2031373

9. Stern PL. Key steps in vaccine development. Ann Allergy Asthma Immunol [Internet]. 2020 Jul;125(1):17–27. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1081120620300715

10. Shrotri M, Swinnen T, Kampmann B, Parker EPK. An interactive website tracking COVID-19 vaccine development. Lancet Glob Heal [Internet]. 2021 [cited 2021 Nov 13];9(5):e590–2. Available from: https://vac-lshtm.shinyapps.io/ncov\_vaccine\_landscape/

11. CDC. Vaccine Testing and Approval Process | CDC [Internet]. Vaccines and Immunizations. 2016 [cited 2021 May 14]. Available from: https://www.cdc.gov/vaccines/basics/test-approve.html

12. Bowman J. Vaccine Development, Testing, and Regulation | History of Vaccines [Internet]. The college of Physicians of Philadelphia. 2016 [cited 2021 May 16]. Available from: https://www.historyofvaccines.org/content/articles/vaccine-development-testing-and-regulation%0Ahttps://www.historyofvaccines.org/content/articles/vaccine-development-testing-and-regulation%0Ahttps://www.historyofvaccines.org/content/articles/vaccine-deve

13. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet (London, England) [Internet]. 2020;395(10223):497–506. Available from: http://www.ncbi.nlm.nih.gov/pubmed/31986264

14. Han S. Clinical vaccine development. Clin Exp Vaccine Res [Internet]. 2015 Jan;4(1):46–53. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25648742

15. World Health Organization Ethics and COVID-19 Working Group. Vaccines/COVID-19 vaccine EUL issued | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control) [Internet]. 2021 [cited 2021 Nov 13]. Available from: https://extranet.who.int/pqweb/vaccines/vaccinescovid-19-vaccine-eul-issued

16. U.S. Food and Drug Administration (FDA). Emergency Use Authorization for Vaccines Explained [Internet]. 2020 [cited 2021 Feb 14]. Available from: https://www.fda.gov/vaccines-blood-biologics/vaccines/emergency-use-authorization-vaccines-explained

17. WHO. Regulation and Prequalification [Internet]. World Health Organisation (WHO). 2021 [cited 2021 May 14]. Available from: https://www.who.int/teams/regulation-prequalification/eul/

18. World Health Organization (WHO). Coronavirus disease (COVID-19): Use of Emergency Use Listing procedure for vaccines against COVID-19 [Internet]. 2021 [cited 2021 May 15]. Available from: https://www.who.int/news-room/q-a-detail/coronavirus-disease-use-of-emergency-use-listing-procedure-forvaccines-against-covid-19

19. World Health Organization (WHO). Coronavirus disease (COVID-19): Vaccines [Internet]. 2021 [cited 2021 Jun 23]. Available from: https://www.who.int/news-room/q-a-detail/coronavirus-disease-(covid-19)-vaccines

20. Jecker NS, Wightman AG, Diekema DS. Vaccine ethics: an ethical framework for global distribution of COVID-19 vaccines. J Med Ethics [Internet]. 2021 Feb 16;medethics-2020-107036. Available from: https://jme.bmj.com/lookup/doi/10.1136/medethics-2020-107036

21. Bowen RAR. Ethical and organizational considerations for mandatory COVID-19 vaccination of health care workers: A clinical laboratorian’s perspective. Clin Chim Acta [Internet]. 2020 Nov;510:421–2. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0009898120303855

22. World Health Organization Ethics and COVID-19 Working Group. COVID-19 and mandatory vaccination : Ethical considerations and caveats [Internet]. 2021 p. 13–7. Available from: https://apps.who.int/iris/rest/bitstreams/1342697/retrieve

23. UNESCO. Universal Declaration on Bioethics and Human Rights [Internet]. 2005 [cited 2021 Jan 1]. Available from: http://portal.unesco.org/en/ev.php-URL\_ID=31058&URL\_DO=DO\_TOPIC&URL\_SECTION=201.html

24. NHS Mid Essex CCG. COVID-19 Vaccination Consent Forms and Letters [Internet]. 2021 [cited 2021 Feb 23]. Available from: https://midessexccg.nhs.uk/medicines-optimisation/covid-19-resources/covid-19-vaccination-resources/covid-19-vaccination-consent-forms

25. NHS Mid Essex CCG. COVID-19 vaccination: easy-read consent form for adults - GOV.UK [Internet]. 2021 [cited 2021 May 8]. Available from: https://www.gov.uk/government/publications/covid-19-vaccination-easy-read-consent-form-for-adults

26. Law LS-C, Lo EA-G. Counselling for COVID-19 vaccine is necessary: Balancing the autonomy, beneficence and non-maleficence in the context of accelerating vaccine development. Int J Clin Pract [Internet]. 2021 Jun;75(6):e14015. Available from: http://www.ncbi.nlm.nih.gov/pubmed/33998757

27. Moodley K, Hardie K, Selgelid MJ, Waldman RJ, Strebel P, Rees H, et al. Ethical considerations for vaccination programmes in acute humanitarian emergencies. Bull World Health Organ [Internet]. 2013 Apr 1;91(4):290–7. Available from: http://www.who.int/entity/bulletin/volumes/91/4/12-113480.pdf

28. McAdams D, McDade KK, Ogbuoji O, Johnson M, Dixit S, Yamey G. Incentivising wealthy nations to participate in the COVID-19 Vaccine Global Access Facility (COVAX): a game theory perspective. BMJ Glob Heal [Internet]. 2020 Nov 30;5(11):e003627. Available from: https://gh.bmj.com/lookup/doi/10.1136/bmjgh-2020-003627

29. The Lancet. Access to COVID-19 vaccines: looking beyond COVAX. Lancet [Internet]. 2021 Mar;397(10278):941. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673621006176