Frequently Asked Questions (FAQs) about COVID-19 Candidate Vaccines and Access Mechanisms

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Document subject to revision as new evidence and information become available

Progress in the Development of COVID-19 Vaccines

1. **Is there a vaccine against COVID-19?**
   At this moment, there are no SARS-CoV-2 vaccines licensed by the World Health Organization (WHO), the virus causing the COVID-19 pandemic. As of 25 August 2020, there are 31 candidate vaccines in clinical evaluation in humans and 142 candidate vaccines in the preclinical phase. The landscape of COVID-19 vaccines is updated on a regular basis by WHO at the following link: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

2. **Will all the COVID-19 candidate vaccines be successful?**
   Only a portion of candidate vaccines will be successful. A study about vaccines targeting human infectious diseases showed that candidate vaccines in preclinical evaluation have an estimated marked entry probability of 7%, and once they have entered clinical evaluation of 17%.[2] In coming years, it is likely that COVID-19 vaccines will gradually become available.

3. **What are the different phases a vaccine must go through to be approved?**
   The evaluation of a vaccine candidate undergoes different phases (preclinical and clinical) until a vaccine receives regulatory approval[3]. The objective of this entire process is to ensure a safe and effective vaccine (as well as to answer other questions like dose number and timing).

   - **Preclinical phase:** focuses on testing vaccine safety and its ability to produce an immune response in animals.

   The clinical evaluation in humans includes:

   - **Phase 1:** trials are held on a small number of humans – usually under 100 adults – to evaluate the vaccine's safety and its ability to generate an immune response (immunogenicity). This phase could include studies to determine the number of doses needed and the methods of administering the vaccine. If the vaccine proves to be safe during phase 1, it will advance to phase 2.

[1] A previous version of the document was published on 3 April 2020: https://iris.paho.org/handle/10665.2/52273
[2] Pronker ES, Weenen TC, Commandeur H, Claassen EH, Osterhaus AD. Risk in vaccine research and development quantified. PLoS One. 2013;8(3):e57755. doi:10.1371/journal.pone.0057755
[3] https://www.paho.org/es/documentos/covid-19-fases-desarrollo-vacuna

- **Phase 2:** the number of humans the vaccine is tested on increases to usually between 200 and 500. The vaccine is given to people who present characteristics (such as age and physical health) like those for whom the new vaccine is intended. During this phase, scientists will continue assessing its safety and capacity to generate an immune response.
- **Phase 3:** the candidate vaccine is tested on several thousands of people. Phase 3 trials focus on assessing efficacy, are randomized and double-blind (meaning those participating in the studies do not know if they receive the real vaccine or a placebo) and can include single and multi-country studies. This phase is usually the last step before the vaccine receives the regulatory approval for vaccination of the population.

After the vaccine is approved, it is also submitted to strict and continuous monitoring. The countries rely on surveillance systems to monitor adverse events. Additionally, many vaccines undergo a **Phase 4** to assess effectiveness and monitor rare adverse events that may occur on an extremely rare basis, e.g. one in 2-3 million doses.

4. **In which clinical evaluation phase are the most advanced COVID-19 candidate vaccines?**
   As of 25 August 2020, there are six COVID-19 candidate vaccines in phase 3 (details are provided in Table 1). There is no direct correlation between the trial phase of vaccine and its superiority or future success. A vaccine reaching phase 3 would not necessarily indicate that it is better than a vaccine in phase 1 or phase 2. At the same time, it is important to consider that not all vaccine manufacturers with products in clinical studies have the capacity to scale up their production and distribution to respond to global demand.

5. **How long does it take to develop a vaccine? When will COVID-19 vaccines be available?**
   The development of a novel vaccine is a complex and lengthy process that on average takes 10 years. Given the current COVID-19 pandemic, institutions, commercial developers, and researchers around the world are working at an unprecedented speed and scale targeting for safe and effective COVID-19 vaccine(s) in approximately 12-18 months. Preliminary results of phase 3 vaccine trials might be available by the end of 2020; however, it is unlikely that WHO pre-qualified vaccines will be available by then.

6. **Where are these COVID-19 candidate vaccines being developed?**
   Most of the companies and institutions developing vaccines against COVID-19 are in countries such as the United States of America, United Kingdom, and China. However, some of the vaccine clinical trials will take place in clinical sites in countries in Latin America (e.g. Argentina and Brazil).

7. **What types of COVID-19 vaccines are being developed?**
   Various technologies and platforms are being used such as:

- **Nucleic acids (DNA, RNA) vaccines:** vaccines that use one or more of the coronavirus's own genes to provoke an immune response.
- **Viral vector vaccines:** vaccines that use a virus – non-replicating or replicating vector – to deliver coronavirus genes into cells and provoke an immune response.
- **Protein-based vaccines:** vaccines that use a coronavirus protein or a protein fragment (protein sub-unit) to provoke an immune response.
- **Whole-virus vaccines:** vaccines that use a weakened (attenuated) or inactivated version of the coronavirus to provoke an immune response.

Table 1: Description of the Six COVID-19 Candidate Vaccines That Are in Phase 3 Clinical Trials (WHO landscape of 25 August 2020)

Developer (country)	**Sinovac (China)**	**Wuhan Institute of Biological Products/Sinopharm (China)**	**Beijing Institute of Biological Products/Sinopharm (China)**	**University of Oxford /AstraZeneca (UK)**	**Moderna /NIAID (US)**	**BioNTech/Fosun Pharma/Pfizer (US)**
Name of candidate vaccine	Sinovac vaccine	CNBG Wuhan	BBIBP-CorV	ChAdOx1-S	mRNA-1273	BNT162b
Platform	Inactivated	Inactivated	Inactivated	Non-replicating viral vector	RNA	RNA
Objective	Safety and efficacy	Safety and efficacy	Safety and efficacy	Safety, efficacy, and immunogenicity	Safety, efficacy, and immunogenicity	Safety, efficacy, immunogenicity, and tolerability
Study design	Phase 3, double-blind randomized, 8,870 participants ≥18 years (healthcare professionals), 2 doses (0, 14 days), IM. Location: Brazil (collaboration with Butantan Institute). Primary	Phase 3, double-blind randomized, 15,000 participants ≥ 18 years, 2 doses (0, 14 days or 0, 21 days), IM. Location: United Arab Emirates. Primary completion date: 15/07/21	Phase 3, double-blind randomized, 15,000 participants ≥ 18 years, 2 doses (0, 14 days or 0, 21 days), IM. Location: United Arab Emirates. Primary completion date: 15/07/21	Phase 3, blind randomized, 10,260 participants ≥18-55 years, 1 dose, IM. Location: UK, Brazil (collaboration with Fiocruz-BioManguinhos), and the USA. Primary completion date: 1/10/21	Phase 3, double-blind randomized, 30,000 participants ≥ 18 years, 2 doses (0, 28 days). Location: USA. Primary completion date: 27/10/22	Phase 3, triple-blind randomized, 28.481 participants 18-85 years, single or 2 doses (0, 28 days). Location: Argentina, Brazil, USA. Primary completion date: 16/04/21

	completion date: 30/09/21					
Trial registry number (link)	NCT04456595	ChiCTR2000034780	ChiCTR2000034780	SRCTN89951424 NCT04516746	NCT04470427	NCT04368728
Status	Participant registration	Participant registration	Participant registration	Participant registration	Participant registration	Participant registration

Note: Single blind trial: only the researcher knows whether a participant is receiving placebo or vaccine. Double blind trial: neither the participants nor the researchers know who is receiving placebo or vaccine. Triple blind trial: neither the participants nor the researchers nor the individuals who assess the outcomes know who is receiving placebo or vaccine.

Characteristics of COVID-19 Candidate Vaccines

8. What will be the presentation of the COVID-19 vaccines?

This information is still unknown; however, vaccines will likely come in multidose packaging.

9. How many doses will be needed?

This information is still unknown. Ongoing COVID-19 vaccine candidate clinical trials are considering whether one, two, or multiple doses are needed. If more than one dose is required, the number of weeks or months between doses is still being researched.

10. What could be the cold chain requirements of COVID-19 vaccines?

While most of the COVID-19 candidate vaccines are expected to present similar cold chain requirements as existing vaccines (between 2-8°C), those developed using nucleic acids (DNA or RNA) might require lower temperatures such as -70°C or -80°C.

11. What could be the administration routes of COVID-19 vaccines?

The COVID-19 candidate vaccines in preclinical and clinical evaluations are using different administration routes. The specified WHO Target Product Profile (TPP) (https://www.who.int/publications/m/item/who-target-product-profiles-for-covid-19-vaccines) describes the preferred and minimally acceptable profiles for human COVID-19 vaccines, and indicates that any route of administration is acceptable, including intramuscular or subcutaneous injection, oral or intranasal.

12. Will it be possible to co-administer COVID-19 vaccines with other existing vaccines against other pathogens?

This information is still unknown. Future studies will assess it.

13. Will it be the same COVID-19 vaccine for pediatric and adult uses?

This information is still unknown. The ongoing clinical trials of COVID-19 vaccine candidates are including general at-risk population, healthy adults, elderly, children, people who are HIV+, and health care workers.

Access to COVID-19 Vaccination

14. Who will be the priority population groups to receive COVID-19 vaccination first?

When a vaccine against COVID-19 becomes available, there will be a huge demand and supply will be limited. Priority populations for the first round of vaccinations will be defined based on the vaccination goal: a) protect the health system and allow the continuity of essential health services (likely include essential workers, including healthcare workers), b) reduce severe COVID-19 morbidity and mortality in high-risk groups (adults over the age of 65 and other high-risk adults with underlying health conditions), and c) reduce transmission (vaccination of young adults). WHO's Strategic Advisory Group of Experts (SAGE) on immunization, PAHO's Technical Advisory Group (TAG) on Vaccine-Preventable Diseases, and National Immunization Technical Advisory Groups (NITAGs) will play a key role providing guidance and recommendations. Each country will determine priority groups to vaccinate based on scientific evidence and the pandemic's epidemiological situation.

15. What will be the best vaccine delivery strategy?

Countries should plan for different vaccine strategies to reach the targeted groups. It will be also important for countries to assess their cold chain capacities and sort out their inventory of equipment and training needs. Lessons learned from the delivery of the H1N1 pandemic vaccine and other new vaccine introductions could be leveraged.

16. What will be the price of COVID-19 vaccines?

This information is still unknown and will be based on numerous different complicated factors like: market dynamics, manufacturers' pricing strategy, engagement with any advance market commitment mechanisms, cost of research and development, cost of scaling manufacturing capacities, reliability of demand and risk sharing approaches, etc. Based on initial available information, while some manufacturers are committing to minimal returns (no profit approach) on their pipeline products, other manufacturers indicate their pricing approach to be tiering countries based on income classifications (differentiated prices).

17. What is the ACT-Accelerator?[4]

The Access to COVID-19 Tools (ACT) Accelerator is a mechanism that brings together numerous partners under one global effort to support equal access to the three pillars related to COVID-19: diagnostics, treatments, and vaccines. The vaccine pillar includes three components: development and manufacturing, coordinated by the Coalition for Epidemic Preparedness Innovations (CEPI); policy and allocation, coordinated by WHO; and procurement and delivery at a global scale, coordinated by Gavi with participation from other

[4] The Access to COVID-19 Tools (ACT) Accelerator: https://www.who.int/initiatives/act-accelerator

partners, including WHO. To get more information, please see the following link: https://www.who.int/initiatives/act-accelerator

18. What would be the benefit of a global access mechanism for COVID-19 vaccines?

Three potential situations might present themselves (not mutually exclusive) for a country to consider accessing potential COVID-19 vaccines:

- **National access mechanism:** countries negotiate agreements directly with manufacturers. There is a risk of concentrating the resources in a few potentially unsuccessful COVID-19 vaccine candidates.
- **Grouped access mechanism:** countries from regional groups or blocs negotiate supply agreements with manufacturers. There is also a risk of concentrating the resources in a few potentially unsuccessful COVID-19 vaccine candidates.
- **Global access mechanism:** countries participate in a global mechanism to procure and access COVID-19 vaccines. Participating in a globally coordinated mechanism, countries will be able to hedge the risk and increase chances for success by contributing to a large and diverse portfolio of COVID-19 vaccines. At the same time, through such a global mechanism, governments with limited or no ability to finance their own bilateral procurement can be assured access to life-saving vaccines that would otherwise have been beyond their reach.

19. What is the COVAX Facility?

The COVID-19 Vaccine Global Access (COVAX) Facility represents a global multilateral collaboration intended to accelerate the development, production, and equitable access to COVID-19 vaccines when they become available. For more information, please see the following link: https://www.gavi.org/covid19/covax-facility. To date, nine vaccines are part of the COVAX portfolio, and 172 countries have expressed interest in participating in the COVAX mechanism. For more information, see the following link: https://www.who.int/news-room/detail/24-08-2020-172-countries-and-multiple-candidate-vaccines-engaged-in-covid-19 -vaccine-global-access-facility.

20. What is the Gavi COVAX Advance Market Commitment (AMC)?

Within the COVAX Facility, there are two groupings of countries. The first grouping is composed by the self-financing countries. The second grouping is composed by the 92 countries that may receive a subsidy to help cover the cost of new COVID-19 vaccines. In the Americas, ten countries meet the requirements to receive COVAX AMC support: Bolivia, Dominica, El Salvador, Grenada, Guyana, Haiti, Honduras, Nicaragua, St. Lucia, and St. Vincent and the Grenadines. The list of countries is available at: https://www.gavi.org/news/media-room/92-low-middle-income-economies-eligible-access-covid-19-vaccines-gavi-covax-amc.

To get more information about the Gavi COVAX AMC, see the following link: https://www.gavi.org/sites/default/files/2020-06/Gavi-COVAX-AMC-IO.pdf

21. What is PAHO's Revolving Fund?

PAHO's Revolving Fund for Access to Vaccines is a regional pooled procurement mechanism. For more than 40 years, the Revolving Fund has facilitated demand forecasts and uses of national resources to procure high-quality life-saving vaccines and related products at the most affordable price for countries in the Americas. Currently, 42 Member States and territories benefit from services offered by the Revolving Fund. For more information, please see the following link: https://www.paho.org/en/resources/paho-revolving-fund

22. How is PAHO's Revolving Fund engaged with the COVAX Facility?

As the largest pooled vaccine procurement mechanism in the world for self-financing countries, PAHO contributed to designing the COVAX Facility. In the COVAX Facility Technical Design Document from 11 June, PAHO's Revolving Fund mechanism was recognized as a unified bloc, representing 39 countries that expressed their interest.

23. How will the COVID-19 vaccines be allocated among countries?

A methodology is required to fairly allocate a COVID-19 vaccine, and it will need to prioritize vaccine supply to reduce the impact of the virus as quickly as possible. Global partners are working together to set up the framework and mechanism required to ensure fair allocation through the WHO Fair Allocation Framework and the COVAX Facility. These vaccines will be delivered to all participating countries, in a manner that is proportional to their populations and in a way that they are initially provided to 3% of the population and later expanding to cover up to 20%. Further doses will then be made available based on country need, vulnerability, and COVID-19 threat.

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