Summary on Advances in the Development of Vaccines against COVID-19

3 April 2020

At the end of 2019, the new SARS-CoV-2 coronavirus emerged. Although there is not yet a vaccine against this virus, the field of research for its development is advancing rapidly. In February 2020, the World Health Organization (WHO) convened researchers from all over the world to define the research agenda for SARS-CoV-2 drugs and vaccines, through WHO's Initiative for Research and Development* (R&D Blueprint)[1]. The priorities of the R&D Blueprint agenda for vaccine development include the development of the following elements:

- Animal models in which to evaluate vaccine effectiveness
- Standardized tests to support vaccine development, particularly the evaluation of immune response
- Multi-country protocols for phase 2b/3 clinical trials with the intention of facilitating coordination and efficiency[2]
- Studies of potency and production processes so that large quantities of vaccines can be produced

WHO will also develop a Target Product Profile (TPP), with the intention of defining the expectations and expected characteristics of the vaccine, as well as a web platform to share information.

In this context, the Coalition for Epidemic Preparedness Innovations (CEPI) is mobilizing resources for vaccine development to increase the chances of success and to finance clinical trials of some candidate vaccines against SARS-CoV-2. The intention is to have some candidate vaccines that can be submitted to regulatory authorities for approval for general use or for use in outbreak situations.

There are currently 54 vaccine candidates for COVID-19, 51 candidates in the preclinical phase, and three have initiated phase 1 clinical trials in humans.[3] This advance is a historical milestone, compared to the development of other vaccines against emerging diseases such as SARS, influenza A (H1N1), and Ebola. For example, it took 20 months to start the first human trials for the SARS vaccine in 2003, four months for the influenza A (H1N1) vaccine in 2009, while the first candidate vaccine against SARS-CoV-2 took just two months, from virus sequencing to administration of the first vaccine in a human clinical trial.

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[1] https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus/en/

[2] https://www.who.int/blueprint/priority-diseases/key-action/COVID-19-vaccine-trial-synposis.pdf?ua=1

[3] https://www.who.int/blueprint/priority-diseases/key-action/Novel_Coronavirus_Landscape_nCoV_Mar26.PDF?ua=1

Various technologies and platforms are being used such as nucleic acids (DNA, mRNA), viral vector vaccines, inactivated vaccines, protein subunit vaccines, attenuated vaccines, intranasal vaccines, oral vaccines, among others. Some of these technologies had been used to develop vaccines for other coronaviruses (such as SARS, MERS) and tested on animals.

The following table[4] describes the platforms, attributes, and statuses of vaccine candidates, including dosages, licenses for the platform, speed at which it can be developed, and large-scale production capacity.

Vaccine Platforms, Their Attributes, and the Status of Vaccine Candidates.*

Technology	Attributes				Candidates in Preclinical Development	Candidates in Phase I
	Single Dose	Licensed Platform	Speed	Current Scale		
DNA	No	No	Fast	Medium	Inovio Pharmaceuticals Takis/Applied DNA Sciences/Evvivax Zydus Cadila	
Inactivated	No	Yes	Medium	Medium to high	Sinovac	
Live attenuated	Yes	Yes	Slow	High	Codagenix/Serum Institute of India	
Nonreplicating vector	Yes	No	Medium	High	GeoVax/BravoVax Janssen Pharmaceutical Companies University of Oxford Altimmune Greffex Vaxart ExpresS2ion	CanSino Biologics (ChiCTR2000030906)
Protein subunit	No	Yes	Medium to fast	High	WRAIR/U.S. Army Medical Research Institute of Infectious Diseases Clover Biopharmaceuticals Inc/GSK Vaxil Bio AJ Vaccines Genrex/EpiVax/University of Georgia Sanofi Pasteur Novavax Heat Biologics/University of Miami University of Queensland/GSK/ Baylor College of Medicine iBio/CC-Pharming	
Replicating viral vector	Yes	Yes	Medium	High	Zydus Cadila Institut Pasteur/Themis Tonix Pharma/Southern Research	
RNA	No	No	Fast	Low to medium	Fudan University/Shanghai JiaoTong University/RNACure Biopharma China CDC/Tongji University/Stermina Arcturus/Duke-NUS Imperial College London Curevac BioNTech/Pfizer	Moderna/NIAID (NCT04283461)
Uncertain					University of Pittsburgh University of Saskatchewan ImmunoPrecise MIGAL Galilee Research Institute Doherty Institute Tulane University	

* Attributes refer to general attributes of the platform, and assessments are not intended as inferences about a particular candidate. NIAID denotes National Institute of Allergy and Infectious Diseases, and WRAIR Walter Reed Army Institute of Research.

The three vaccines that are in a phase I clinical trial as of 3 April 2020 are briefly described below:

1) **Company:** Moderna from Cambridge, Massachusetts in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID), which is part of the National Institutes of Health (NIH).

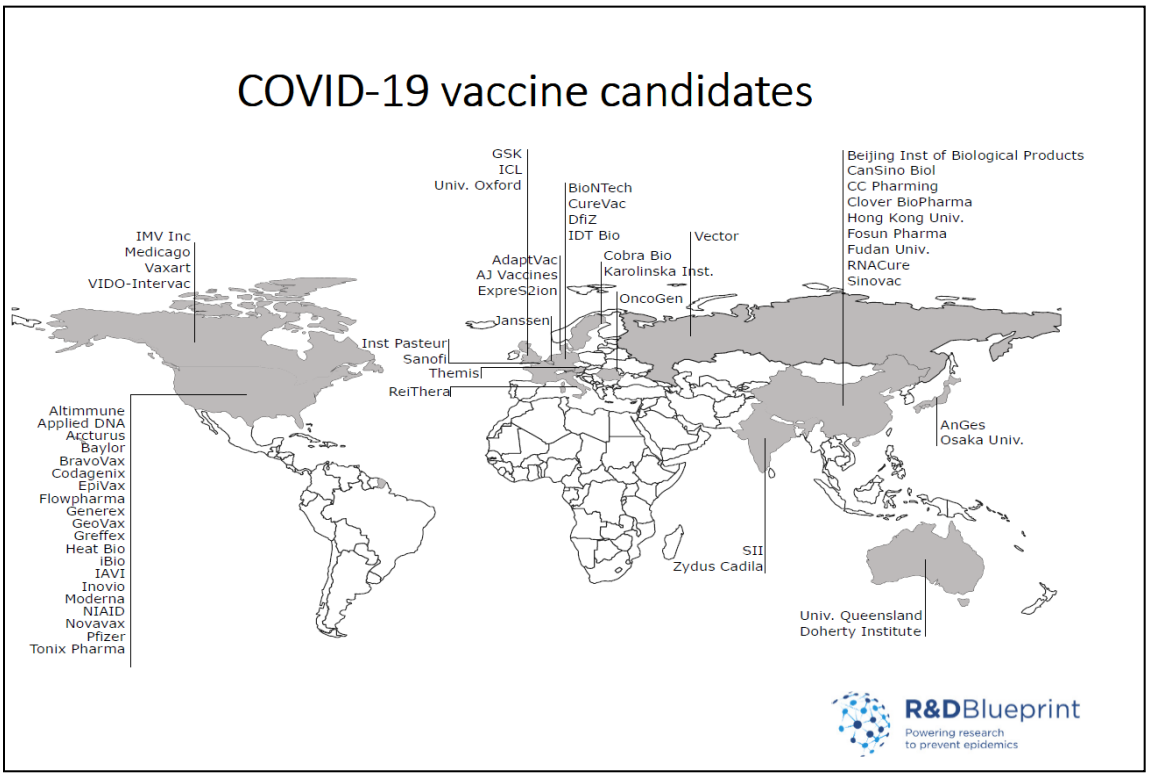
[4] https://www.nejm.org/doi/full/10.1056/NEJMp2005630

Name of the candidate vaccine: mRNA-1273, developed based on previous studies with SARS and MERS.
Description: It uses a synthetic chain of messenger RNA (mRNA), designed for cells to make antibodies against the virus.
Study design: Phase 1, open, use of different doses in 45 healthy adult volunteers aged 18-55 years.
Status: The recruitment process began on 16 March and was completed on 19 March. The study evaluates different doses of the experimental vaccine considering safety and immunogenicity. Moderna has indicated that the vaccine could be commercially available in the United States in 12-18 months, although it has already applied for a permit for use in an emergency that could allow its use before it is licensed.
More information: https://www.modernatx.com/modernas-work-potential-vaccine-against-covid-19

2) **Company:** CanSino Biological Inc. and Beijing Institute of Biotechnology of China
Name of the candidate vaccine: Ad5-nCoV
Description: It uses the same platform used for Ebola (adenovirus viral vector). Its approach is based on taking a fragment of the coronavirus genetic code and interweaving it with a harmless virus, an adenovirus viral vector.
Study design: phase 1, 108 participants between 18 and 60 years old who will receive low, medium, and high doses of vaccine.
Status: Recruitment has started. The study will evaluate safety and tolerability.
More information: http://www.cansinotech.com/

3) **Company:** Oxford University
Name of the candidate vaccine: ChAdOx1
Description: A team of researchers at the Jenner Institute at Oxford University, who had been working on MERS vaccines, quickly adapted the technology to produce a vaccine against the new coronavirus SARS-CoV-2.
Study Design: Phase 1, 510 healthy adult volunteers ages 18 to 55.
Status: It is currently recruiting participants.
More information: https://www.ovg.ox.ac.uk/

The following map shows the worldwide distribution of companies and institutions developing vaccines against the new SARS-CoV-2 coronavirus:



Conclusions

There are many scientific and technical challenges in vaccine development to achieve vaccines that are safe and effective, including the requirement of time and investment of resources. It has been two months since the declaration of the pandemic and more than 50 companies, universities and research institutions globally have joined in an unprecedented collaborative effort to develop a vaccine to face the COVID-19 pandemic. Vaccines approved for use in humans are expected to be available in a period of 12 to 18 months.

Once vaccines are developed, the Region of the Americas will have to face other important challenges, like guaranteeing equitable access to the vaccines for all the countries of our Region. The PAHO Revolving Fund will play a key role in negotiating vaccines on behalf of the countries, as it did during the influenza A (H1N1) pandemic, which resulted in earlier access to pandemic vaccines compared to other WHO regions.

Immunization advisory groups such as WHO's Strategic Advisory Group of Experts (SAGE) on immunization, PAHO's Technical Advisory Group (TAG) on Vaccine-preventable Diseases, as well as National Immunization Technical Advisory Groups (NITAGs), are reviewing the progression of the disease and its highest risk groups to prepare for the introduction of the vaccine, in addition to the generation of evidence to make evidence-based technical recommendations for vaccination.

One of the most important aspects during this historical moment to face this pandemic is each country's **preparation** to introduce and deploy this vaccine to the local level in the shortest possible time. Immunization programs should give priority to the elaboration of national vaccination plans, as well as having the necessary infrastructure, including the cold chain and information systems.

The Region has important lessons learned from the 2009 influenza pandemic, as well as annual seasonal influenza vaccination, which will be utilized for vaccination against COVID-19, to vaccinate risk groups, such as older adults, people with chronic diseases and health workers, among others. A key aspect of preparedness is having strengthened epidemiological surveillance systems, including active surveillance at sentinel sites for surveillance of adverse events supposedly attributable to vaccination or immunization (ESAVIs).

The Region has also made progress in evaluating the effectiveness and impact of influenza vaccines through the REVELAC-i and SARINET networks, which will be adapted for the evaluation of this vaccine. PAHO will be providing the technical cooperation required by countries in the process of preparing, implementing, and evaluating vaccination against COVID-19.

Reference number: PAHO/FPL/IM/COVID-19/20-0009