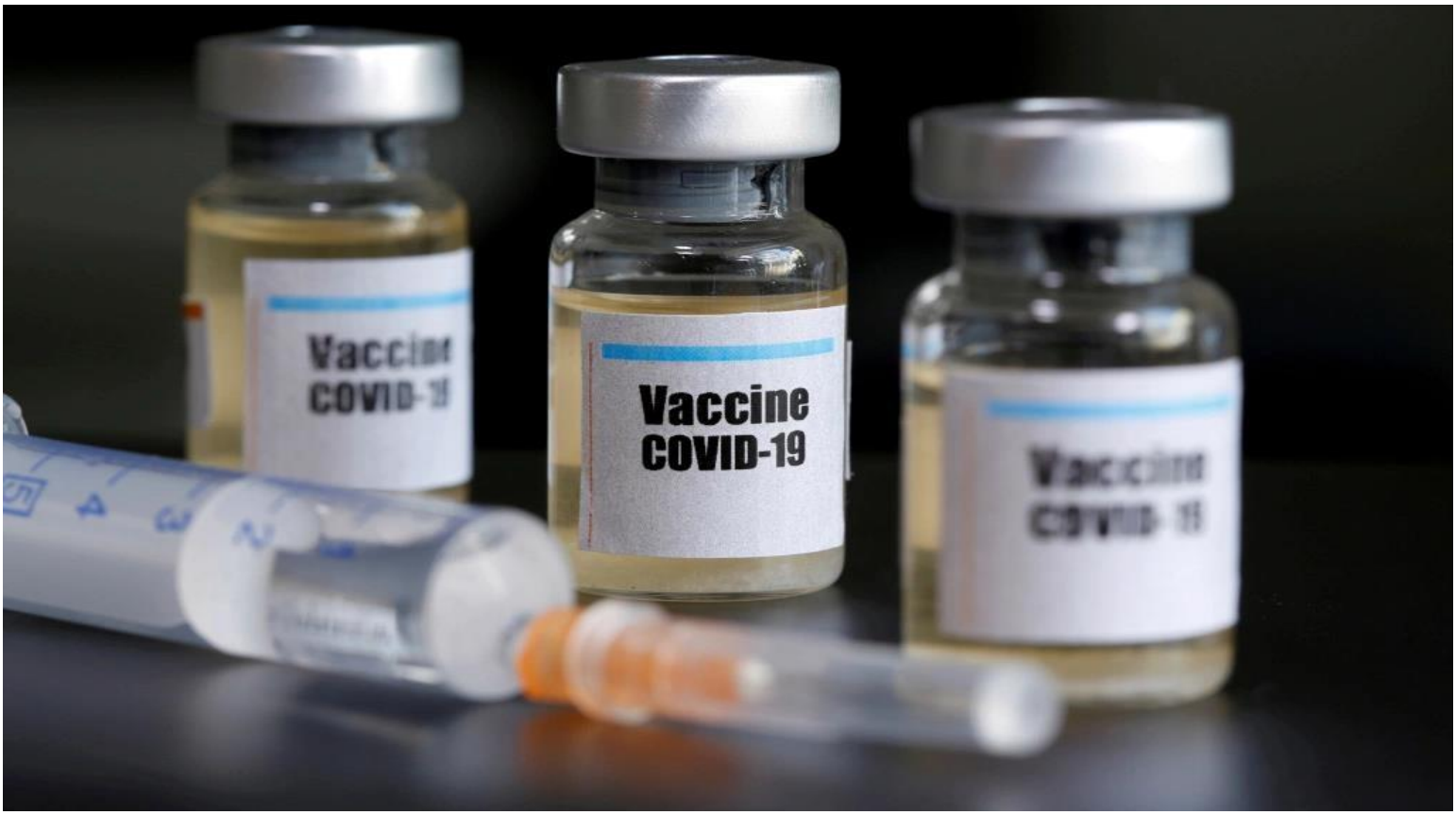
PARLIAMENTARY ASSEMBLY OF THE MEDITERRANEAN
ASSEMBLEE PARLEMENTAIRE DE LA MEDITERRANEE
الجمعية البرلمانية للبحر الأبيض المتوسط

# BRIEF ON COVID-19 VACCINE

Geneva, 18 August 2020

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## Purpose

This paper provides information and analysis[1] for PAM parliamentarians and the staff of PAM's Members and Partners in relation to the latest state of knowledge and action with regard to vaccination on COVID-19, and also recommends core actions for them to consider to promote fair and equitable access, when a safe and effective vaccine becomes available.

## Introduction

By later August 2020, some 22 million COVID-19 worldwide infections had been reported including around 800,000 deaths; these numbers are likely under-estimates and true figures may be ten times greater.

The pandemic has extracted huge personal, social, and economic costs – directly and indirectly. This is set to continue until societies learn to live and function in the continuous and permanent presence of the virus. How can that happen?

## Population immunity

The virus will be controlled until at least 60-70% of people have become immune to the virus, thereby checking its relentless propagation. Such a level of population immunity can happen in two ways:

- First, either by more and more people acquiring the naturally-circulating virus, with a significant proportion getting mildly and moderately (80%) or seriously (10-20%) sick with a tiny fraction (0.5%) dying.
- Second, by inducing "artificial immunity" through vaccination against the coronavirus (SARS-COV-2) that causes COVID-19.

As the virus is new to humans, no one had immunity to it when it started spreading outwards from its origin, supposedly during late 2019, in Wuhan, China. We also don't know enough about the nature of human immunity in relation to this virus. The 'immunity mechanisms' are still being unravelled; they are likely to involve both antibodies and a cellular pathway (T-cells) but their relative importance is not clear yet. The critical question here is the strength and length of the immunity developed by a person who acquires the virus.

After at least 9 months of progressive spread, we do not yet know the proportion of the world population that has acquired immunity from natural exposure. But it is quite small: perhaps 5- 15% in most places.

While this proportion of naturally acquired immunity will continue to grow, it will take a very long time to get to the desirable population immunity threshold level of 70% and, along the way, many more people could get seriously ill and die.

Understandably, waiting for natural immunity to take its course is considered morally and politically unacceptable. Hence, the huge interest and investment in developing a vaccine against the coronavirus to quickly boost population immunity and provide a long-term solution to managing the virus.

## Developing a vaccine

A vaccine mimics the virus or part of it and protects against it by stimulating the immune system to develop antibodies.

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[1] *This is an advisory note based on the best available knowledge at the time of writing. As the COVID-19 pandemic is a fast-moving emergency caused by a new virus the scientific understanding of which is evolving, this note may need to be updated as appropriate*

Normally, developing a vaccine takes several years and efforts are not always successful. However, COVID-19 vaccine research has stimulated huge scientific effort around the world, underpinned by vast levels of investment. The target is to have vaccines being rolled out towards the end of 2020 but that is unlikely to happen and a more possible timeline would be during 2021. However, there is no guarantee that science will succeed in making this happen.

Vaccines must follow higher safety standards than drugs because they are given to millions of otherwise healthy people. Hence, they should not cause harm by making the original disease worse and they must have minimal side-effects while, ideally, they should have a significant protective effect in a large proportion of people.

Therefore, a rigorous testing process has to be followed, data from which should be made openly and transparently available to allow scientific peer review to judge whether a candidate vaccine is effective and safe before it is rolled out for general public use. Such a carefully controlled multi-stage process is as follows:

- In the pre-clinical stage, the candidate vaccine is given to animals to see if it triggers an immune response.
- In phase 1 safety trials, the vaccine is given to a small group of people to determine whether it is safe and to learn more about the immune response it provokes.
- In phase 2 expanded trials, the vaccine is given to hundreds of people, often split into groups such as children and the elderly, to learn more about its safety and correct dosage.
- In phase 3 efficacy trials, the vaccine is given to thousands of people to confirm its effectiveness and safety – including rare side effects that are only picked up when sufficient numbers of people get the vaccine These trials involve a control group which is given a placebo. A coronavirus vaccine would have to protect at least 50% of vaccinated people to be considered effective.

COVID-19 vaccine development is being accelerated by combining some of these phases, but any short-cuts must not compromise efficacy and safety determination. In addition, modern technologies such as artificial intelligence to identify promising molecules and genomic engineering to design them are helping to speed up the process.

In contrast, the rate-limiting step is at phase 3 when thousands of people have to be enrolled and followed-up for many months to test the vaccines. This is proving difficult to do in many countries which already have low rates of the virus circulating in the general population and hence assessing the protective value of the vaccine is difficult Proposals to use human challenge trials by deliberately exposing healthy volunteers to the potentially-lethal virus in order to see if the vaccine stops them from getting infected, have been proposed. But this is ethically contentious under the current circumstances where COVID-19 has no reliable cure.

The vast majority of candidate vaccines are likely to drop out at one or other stage of this process.

The ones that survive the final phase are scrutinised by national regulatory authorities to decide whether or not to approve a vaccine. During an emergency such as the COVID-19 pandemic, a vaccine may get initial ‘emergency use authorization’, before getting full formal approval in due course. As it would be wasteful for the regulatory authorities of every nation to duplicate the essential scrutiny needed, the World Health Organization (WHO) has developed the concept of ‘Stringent Regulatory Authorities (SRA)’ who are trusted as being fully competent in certifying approval. The current SRAs are the regulatory authorities of the European Union, USA, and Japan (and their recognised associates).

Once a vaccine is released for public use, manufacturers are obliged to institute a scheme for post-marketing surveillance that continues to monitor people who receive it to make sure it’s safe and effective, and to detect very rare or unexpected complications that may not emerge for some time. By and large, approved vaccines have a strong history of safety and reliability.

## Current state of COVID-19 vaccine development

Currently, at least 170 vaccines are under research in a dozen or more countries. Different teams have taken different approaches – and that is good for improving the chances of success. It is possible that they may all fail or conversely, result in several effective vaccines. It may then be possible to determine the best vaccine or even to combine more than one approach or more than one vaccine. Of the main vaccines being researched at the time of writing, 138 are in pre-clinical trials, 20 are at phase 1, 11 at phase 2 and 8 at phase 3.

Two vaccines have been approved for use. The one made by CanSino, a Chinese company, was announced in June for emergency use and for use by the Chinese military. The second one is 'Sputnik V', made by Russia's Gamaleya Research Institute, and announced in August. Neither of them have been through phase 3 trials yet and released full scientific data. Their efficacy and safety have not been independently validated as meeting international criteria. As yet, they have not been recommended by WHO nor approved by any of the Stringent Regulatory Authorities.

A few other manufacturers, notably in the UK and US, appear to have products in phase 3 - with some optimism that that their vaccines will be ready at the end of 2020. But only time will tell.

## Vaccine distribution

As and when an effective and safe vaccine or vaccines become available, the challenge of distribution will be faced. As a public health control measure, at least 70-80% of people will need to be vaccinated so as to generate a sufficient level of population immunity that also benefits people who cannot be immunised due to legitimate medical contraindications.

The world is now well-experienced with immunisation programmes and logistics systems to do so are in place in all counties. When the COVID-19 vaccine becomes available it would be expected to piggy-back onto existing systems. While this makes good sense, the stability, storage, and transport requirements of the new COVID-19 vaccines are not clear yet. If they require special handling, it will impose serious challenges for logistics systems.

Meanwhile, existing immunisation capacities are very weak in poorer countries as well as in crisis-affected or so-called 'fragile' states where international help from the Global Vaccine Alliance (Gavi) is usually crucial to ensure adequate coverage.

Weak systems are also wasteful systems: up to 50% of vaccines are wasted every year, often because of inadequate temperature control in supply chains. This is especially crucial for a new COVID-19 vaccine that will be in very short supply. In addition, the marked reduction in international travel has also slowed the movement of cargo. This will need addressing in advance of arranging vaccine distribution. Furthermore, getting the vaccine to rural and remote communities requires special logistics which many poorer countries lack.

In short, unless international and national supply chains are strengthened, it could be several years before vaccines reach everyone who needs them. Meanwhile, diverting logistic capacity towards COVID-19 risks reducing other life-saving vaccination programmes.

## Vaccine uptake

An even more difficult problem is that of 'vaccine hesitancy' which refers to delay in acceptance or even refusal of vaccination despite availability of vaccination services. Vaccine hesitancy is complex, specific to particular contexts, and varies across time and place. It is influenced by factors such as complacency, convenience and confidence. Studies indicate that this could be a significant factor in COVID-19 vaccine uptake.

A major negative influence is the 'anti-vaxxer' lobby of people who are downright hostile. Some 20-30% of people may be in this category in many – especially developed – countries. A segment of vaccine-opposers cite religious or libertarian reasons for opposing vaccines, but mostly the hostility stems from mis- information about vaccination and mistrust in health authorities and governments in general. To overcome that will be a huge challenge for policymakers and opinion-shapers.

**Compulsory vaccination**

Considering the individual and collective benefit, should COVID-19 vaccination be made compulsory? Historical experience is that compulsion does not work in public health and success with any disease control effort is most effective when it seeks voluntary engagement. That is why, despite compulsory vaccination having been tried for several conditions such as smallpox, the resistance stirred-up has been overall self-defeating. In the case of the compulsory vaccination of children before school admission, exceptions allowed for 'philosophical or religious reasons' have had to be allowed or else the children of vaccine- reluctant parents risked victimisation by being denied school education.

COVID-19 has already extracted huge costs in terms of the erosion of human rights and liberties and this has been particularly worrisome in authoritarian states. With the prevalent lack of trust in governments and health experts in so many places, compulsory vaccination measures are likely to require considerable coercive enforcement which will further undermine trust, especially in the other public health measures which are equally essential in the control of COVID-19.

There may a very limited case for occasional exception to this under special institutional circumstances experiencing an outbreak e.g. hospitals, old peoples' homes, army camps, and prisons. Also, it may be considered in serious community outbreaks with a very large number of vulnerable people. But even there, voluntary encouragement is much preferred.

In short, compulsory approaches to general COVID-19 vaccination may do more net harm than good, and are not recommended.

**Vaccine access**

Depending on whether 1, 2, or 3 injections are required for the initial protection of a person, we would need at least 15 billion doses of the vaccine. This is roughly twice the world's current total vaccine manufacturing capacity and could also mean shortages of other vaccines such as those for childhood diseases. Thus prioritising COVID-19 vaccines could cost many other lives from other vaccine-preventable causes.

Several manufacturers are expanding production capacities by establishing links with the original patent holders of the successful vaccines and agreeing to make them in many different places under license. In several cases, manufacturing has already started even though the vaccine has not been certified as effective. There is the risk that if that never happens, the manufactured doses will have to be destroyed, and the investment made wasted.

In the future, a further way to expand availability of the vaccine for developing nations would be to invoke the flexibility allowed under the Doha Declaration on the 'Agreement on Trade- Related Aspects of Intellectual Property Rights (TRIPS) and Public Health' to allow lower income countries to over-ride patents and invoke the compulsory licensing of essential life- saving medicines and vaccines in case of a national public health emergency such as a disease epidemic. The big pharmaceutical companies and the rich Western nations (where they are usually based) do not like developing countries to invoke the 'TRIPS flexibility' provision and this may become a source of international tension.

Meanwhile, fearing a shortage of potential vaccines (in the same way that medicines, ventilators, and personal protective equipment – PPE - fell very short during the early months of the pandemic, several

high-income countries have scrambled to sign advance purchase agreements with vaccine manufacturers to guarantee access. These are commercially confidential agreements signed in secret, often with different prices being charged to different governments. The implication is that countries that can afford to buy vaccine stocks in advance will get first access, leaving poorer nations to miss out or be obliged to wait.

This has been dubbed ”vaccine nationalism” and goes against global calls for the equitable sharing of successful COVID-19 vaccines.

**Equitable vaccine access**

Concerned that poorer countries will not be able to access life-preserving COVID-19 diagnostics, therapeutics and vaccines in a timely manner, WHO has developed the ‘ACT- Accelerator’ as a partnership of key stakeholders in the public and private sector, so as to accelerate their development, production and equitable access.

Within the ACT-Accelerator, sits ‘COVAX’ which is co-led by Gavi, the Coalition for Epidemic Preparedness Innovations (CEPI) and WHO. This aims to accelerate the development and manufacture of COVID-19 vaccines, and to guarantee fair and equitable access by every country. Such equity is important because, worldwide, “no one will be safe until all are safe”.

However, as vaccine availability is going to be limited, even under the most optimistic scenarios, the most efficient policy is to prioritize the most vulnerable groups earlier than the general population.

Hence, the following should be given first access:

- health care workers (1% of the global population of 7.5 billion)
- adults over 65 years old (8%)
- other high-risk adults with underlying conditions eg. hypertension, diabetes, etc. (15%)

Some of the above categories will overlap but some additional supplies also need to be kept in reserve for emergencies i.e. for vaccinating everyone in a particular community when a major outbreak happens somewhere within it.

Therefore, in broad figures, around 2 billion initial doses of COVID-19 vaccines should be reserved worldwide for public health priority allocations, available to all countries. This equates to approx 20% of the population of every country. The COVAX facility has estimated its total immediate funding need at US$18.1 billion, to deliver 2 billion COVID-19 vaccines by the end of 2021.

In summary, joining the COVAX facility entitles each country to get enough vaccine – as soon as it is available - to cover 20% of its population (most needy segment). Subject to donor funds received, low and lower middle income countries will get the vaccine free or at highly subsidised rates. Richer (upper middle income and upper income countries) nations will also get their 20% allocation if they have joined COAX – but would have to finance this themselves.

This translates to the following in case of PAM member states:

- **Syria** (LIC) and **Algeria, Egypt, Mauritania, Morocco, Tunisia** (all LMICs) should be able to get free or highly subsidised access.
- At the time of writing, the richer and self-financing countries that have expressed formal interest in the COVAX facility are **Andorra, Croatia, Greece, Israel, Jordan, Lebanon, Monaco, Montenegro, North Macedonia, Portugal**, **Slovenia**.
- At the time of writing, the views of **Albania, Bosnia and Hercegovina, Cyprus, France, Italy, Libya, Malta, Palestine, Romania, Serbia, Slovenia, Turkey** were not formally

expressed in terms of their interest in benefitting from COVAX.

## PAM parliamentarians' role

Parliamentarians in PAM have an important leadership role through policy development and advocacy, to help ensure that populations in their own and other countries will have equitable access to COVID-19 vaccines when these become available.

Accordingly, parliamentarians are advised to pursue some of the following five key areas of action according to the contexts in which they operate.

**1.** Advocate for, and support initiatives by public health authorities, civil society groups, and media to vigorously fight misinformation and rumour against vaccination, and counter the anti-vaxxer lobby

**2.** Ask for their governments to join-up with COVAX, if they have not already done so.

**3.** Ensure that countries are "vaccination ready" i.e. ready to roll out the COVID-19 vaccine as soon as it is available. This means asking national public health authorities to develop a national COVID-19 vaccination strategy in line with WHO and Gavi guidance, identify the vulnerable groups who should be vaccinated first, and establish adequate logistics to do so.

**4.** For PAM member states in higher and upper middle income countries, urge their governments to contribute generously to the COVAX financing facility, if they have not already done so.

**5.** Understand that COVID-19 vaccination, when it arrives, is only one tool in the struggle against the pandemic, and continue to lobby and advocate for investing in and strengthening wider public health and public education systems for the long-term prevention and control of this and future disease outbreaks.

Parliamentarians and their staff may request the PAM Secretariat for education and training inputs and other, more specific advice and assistance in this and related areas of COVID- 19, health and development: to tackle particular bottlenecks and challenges, foster solidarity actions among members, and connect the PAM community for more effective co-operation with regional and global institutions.

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Ref. MK Brief 2