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What Are the Barriers to Achieving Universal Immunisation Against COVID-19?

Series | COVID-19 and response strategy

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[This document is part of a series of discussion notes addressing fundamental questions about the COVID-19 crisis and response strategies. These documents are based on the best scientific information available and may be updated as new information comes to light.]

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All vaccines are based on the same principle: inoculation with an inactivated pathogen or parts of it to train our immune system to recognise the target organism and **generate antibodies that will to protect us against future infections**. However, each pathogen has its own particular characteristics and developing a vaccine against a new virus involves identifying which part of the pathogen should be administered and the best strategy for generating the highest level of immunity for the longest period possible. The development process starts with pre-clinical studies in the laboratory and in animal models before moving on to clinical trials in humans. In phase 1 trials, the safety of the candidate vaccine is tested in a small number of volunteers. In phases 2 and 3, investigators assess the efficacy of the vaccine and confirm its safety on a larger scale. Normally, the **whole process takes at least 10 years and many candidate vaccines are abandoned along the way** because they prove to be either unsafe or ineffective.

In the case of the novel coronavirus vaccine, the aim is **to compress the whole process into an 18-month time frame**. One way to do this is to use strategies that have already been tested with similar viruses. Another approach is to combine the phases to test the vaccine in a larger number of people. This is how **three of the more than 90 coronavirus vaccine candidates have already entered phase 2 trials** following promising but preliminary results in phase 1. However, none of these three candidates use technologies already approved for use in humans: one is based on gene sequences of the virus and the other two use a virus that cannot replicate as a vehicle for delivering coronavirus proteins, a method that presents an additional challenge in that it has never been used before. This makes it even more **important to support the development of a number of differ-**

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ent vaccines, which could ultimately be complementary. Despite the urgency of the situation, the consequences of introducing a vaccine into the market without sufficient guarantees of safety and efficacy would be disastrous for the COVID-19 pandemic and could also fuel the lack of confidence in vaccines that is already affecting a section of the population.

Now, let us suppose that everything goes well and the safety and efficacy of one or more of these vaccines can be demonstrated before the end of the year. This **does not mean that the vaccines will be immediately available to the population**. First we will have to overcome three major obstacles quite unrelated to the purely scientific challenges: **large-scale production**, the **governance of the process**, and the **ownership of the vaccine**.

1. The Challenge of Production

"The coronavirus vaccine will not be available to everyone at the same time. This makes it even more important to ensure fair and equitable distribution of the vaccine through a global system of governance that puts public health criteria before those of the market."

It is one thing to develop a vaccine and quite another to manufacture it at the necessary scale and speed. There are almost seven billion people on the planet with no immunity to the virus. **About four billion doses would be needed to vaccinate at least 50% of the world's population**, a calculation based on the assumption that a single dose confers immunisation and provides life-long protection. In many cases, however, more than one dose is needed to achieve protection, which may only last for a limited period of time.

Many of the companies developing candidate vaccines **do not have large-scale production capacity**. Moreover, the manufacture of a new vaccine often requires specialised equipment and infrastructure and a purpose-built manufacturing facility. Therefore, the race to accelerate production has been started at the same time as the push to advance vaccine research. Although no one knows what the final product will be, the intention is to save time and ensure that the chosen vaccine reaches people as soon as possible. This challenge has given rise to **a number of initiatives around the world, most of them in Western countries**, which have a much greater capacity to develop vaccines than to manufacture them.

In the midst of an electoral campaign, the **US Government** wants to secure its own national production and supply. It has announced an investment of over $1 billion in Operation Warp Speed, a bid to deliver at least 300 million doses—in principle of a vaccine developed by the Jenner Institute at the University of Oxford—by end 2020. This announcement has raised doubts and concern, and many experts consider the deadline to be almost impossible to meet. And, even if the deadline were realistic, it would be impossible in that time frame to confirm the safety of the vaccine with complete certainty or to establish whether it will be more effective than others that may emerge later.

Aware that, at best, current manufacturing capacity could not cover the needs of all countries in a year, the World Health Organisation (WHO) has launched an initiative called *Access to COVID-19 Tools Accelerator or ACT-Accelerator*. One of the pillars of this global project will be the development, manufacture and deployment of a vaccine. Working with the WHO, the Coalition for Epidemic Preparedness Innovations (CEPI) and GAVI, The Vaccine Alliance have a more ambitious goal than the US Government: **to make the vaccine accessible and affordable and to ensure equitable distribution to all the countries in the world, leaving no one behind**.

One of the critical components of this project is the creation of **a funding mechanism that will advance the resources needed** to increase production worldwide by expanding the capacity of existing large vaccine manufacturing fa-

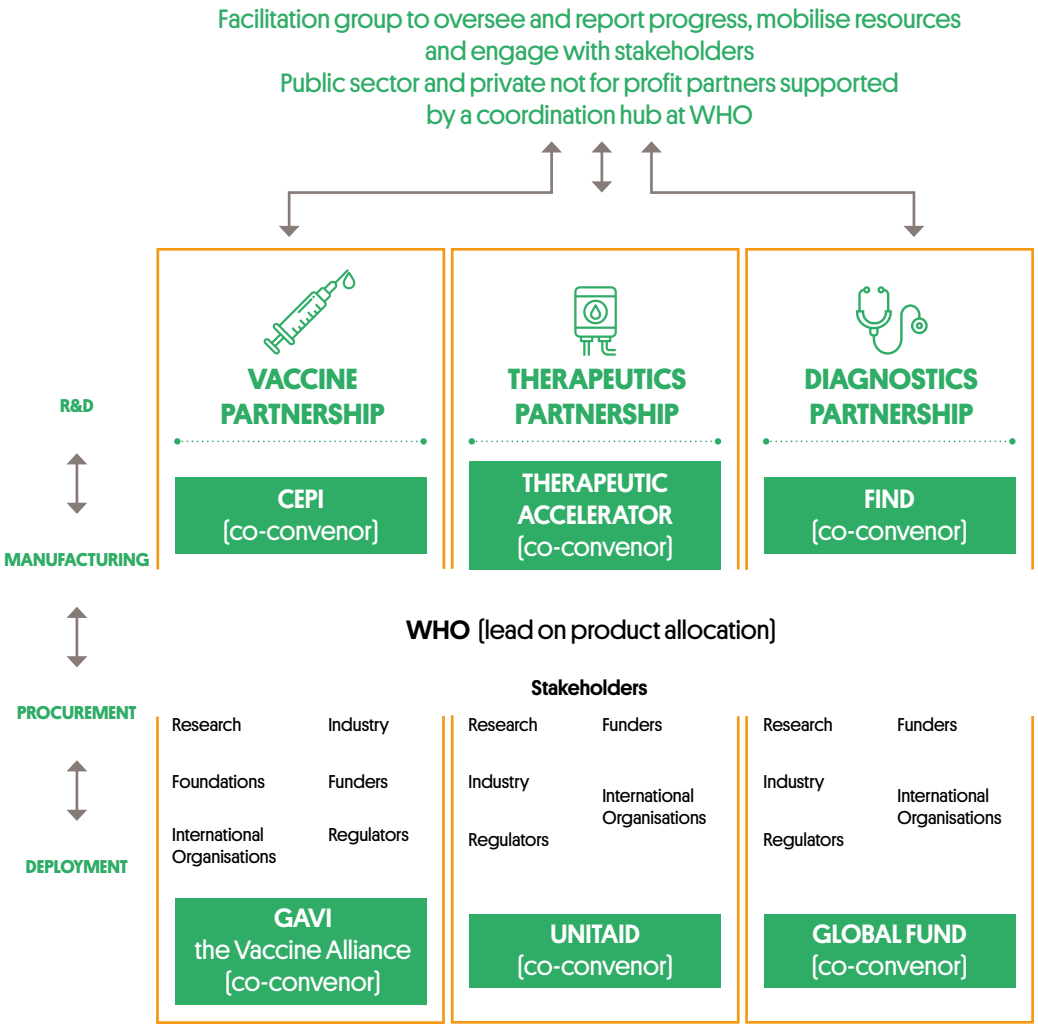
cilities in some middle-income countries with a high technology level, such as India or Brazil, and that of private sector pharmaceutical companies in more advanced economies. The plan is to fund investment in new facilities and means of production in exchange for agreements on the subsequent distribution of the end product. The strategy involves accepting the potential financial risk (since no one knows which vaccine will be effective) in exchange for significant time savings. *(See Figure 1)*

Other obstacles will have to be overcome if we are to produce billions of doses of a vaccine, starting with the challenge of manufacturing a sufficient number of vaccine vials. The current global stock of these vials is around 200 million units, nowhere near the four billion required to ensure worldwide vaccine deployment. These vials are made from a specialised glass designed to keep the contents cool, protecting the vaccine from warmer temperatures that could affect its potency; this makes it difficult to ramp up vial production quickly. Other, no less complicated, problems are to source enough stoppers and syringes to meet the world's vaccine needs and to build the logistical capacity to transport the vaccines at a controlled temperature.

What is clear is that **no single country has the capacity to manufacture so many doses and that a global collaboration involving both the public and private sectors will be needed** to produce billions of doses of coronavirus vaccine(s) over the next three to four years. And all this has to be done while maintaining the production of other necessary vaccines—stocks of which are already inadequate—because a failure to ensure routine immunisation worldwide could cause more deaths than COVID-19.

Given all of the above, it would seem reasonable to suppose that the coronavirus vaccine will not be available to everyone at the same time. This makes **it even more important to ensure fair and equitable distribution** of the vaccine through a global system of governance that **puts public health criteria before those of the market**. If public health interests prevail, international priorities can be set to establish which groups or communities should be immunised first (for example, health care personnel and high-risk individuals). Otherwise, the result would be a massive purchase of the available vaccine by the bidder with the most money to spend, an outcome that would not guarantee control of the pandemic. The aim of vaccination is to protect the individual but also to achieve herd immunity in the population, and it is clear that the risk of SARS-CoV-2 outbreaks will persist so long as transmission of the virus is not controlled in every country ●

Figure 1. ACT-Accelerator: A Global Collaboration Committed to Making a COVID-19 Vaccine Available and Accessible in all the World's Countries.



2. The Challenges of Governance

"The global scope of the pandemic demands a global solution because the persistence of the disease in any part of the world represents a threat to all."

Given the scale and global impact of the COVID-19 pandemic, the international community has highlighted the need to establish mechanisms to ensure that **all countries, including low-income countries, have access to the treatments and vaccines** that are being developed. The role of the WHO is critical in establishing priorities and setting public health standards as well as in defining procedures and supporting their implementation worldwide. However, the WHO is an institution that must answer to 194 member states and their governments, each with its own interests and capacity to act unilaterally. It has no authority over the decisions of member states and lacks the power and resources to create a global consortium to support the manufacture of and universal access to vaccines and treatments.

When the pandemic became **the greatest threat to global security**, a number of proposals were formulated, including one from former British Prime Minister Gordon Brown, who suggested the creation of an organisation with regulatory capacity and the power to impose its criteria

on the health ministries of any country. However, such an outcome seems unlikely at a time when certain countries, such as the USA, are rejecting the multilateral approach and undermining the role of international institutions.

CEPI and GAVI have proposed a different model for making decisions about the vaccine. They propose a more flexible model, funded by the international community and bringing together the capacities of public institutions, technical experts and private organisations (the pharmaceutical industry, private donors and civil society) to implement the policies directly in each country. While CEPI is working on the issues related to the development and manufacture of the most promising candidate vaccines, GAVI is striving to incentivise and finance the production of the vaccines in order to ensure adequate, timely and affordable supplies for low-income countries once a vaccine has been approved. The WHO, on the other hand, will continue to be responsible for developing guidelines and recommendations related to the deployment and administration of the vaccine based on public health criteria.

Through ACT Accelerator, the model proposed for the vaccine will also be used for the development, production and distribution of diagnostic tests and treatments.

The global scope of the pandemic demands a **global solution** because the persistence of the disease in any part of the world represents a threat to all. That is why, ultimately, overcoming the problems involved in production and governance, equitable access and affordability of the vaccines will be closely linked to the third issue: Who owns the vaccine?

3. The Challenge of Vaccine Ownership

"The vast majority of the member states of the WHO Assembly declared that immunisation of the population against COVID-19 should be considered a global public good for health."

In the early stages of research, funding for many of the **vaccine candidates** has come from both public institutions and private, non-profit foundations. However, as the research advances and clinical trials get underway, most of these candidate vaccines become the private property of pharmaceutical companies who have the know-how required to complete these advanced stages. The development and subsequent regulation of the end product will eventually be the deciding factor in who owns the patent, and therefore who will reap the benefits when the approved vaccine goes to market. A **patent** is necessary to guarantee a return to investors, but it could also raise critical barriers to the global deployment of the end product. The first barrier is that a patent results in a price that is affordable for some countries but not for others; the second, no less important, obstacle is that the patent prevents or delays the transfer of knowledge to manufacturers who could accelerate production anywhere in the world.

In a proposed resolution, the vast majority of the member states of the WHO Assembly declared that immunisation of the population against COVID-19 should be considered a global public good for health and that **global access to the vaccine for all** should be ensured by making use of the public health safeguards inherent in current trade and intellectual property agreements.

In practice, the adoption of such a resolution would imply ignoring the patent, sharing knowledge, and scaling up global production. However, when the petition was presented to the WHO Assembly, the resolution that was to have recognised the COVID-19 vaccine as a global public good ended up **as a generic reference to immunisation**. The change was made to gain the support of some of the countries that are key players in the distribution of vaccines and medicines worldwide, such as Great Britain. Even with the modification, the resolution was

not signed by the United States, which considered that the ownership of the vaccine should remain in private hands and its distribution be achieved through the usual market mechanisms.

At this stage, there are several possible options:

- **Create a vaccine not subject to any patent**, a solution very likely to discourage the pharmaceutical industry from undertaking its share of the work.

- Apply formulas used previously with other medicines, such as **setting different prices depending on the income** of the country procuring the product (differential pricing).

- Make use of the exceptions provided for in the *Agreement on Trade-Related Aspects of Intellectual Property Rights* (TRIPS, 1995), including the flexibilities recognised in the Doha Declaration (2001), which allow countries to use **compulsory licensing to authorise the manufacture of treatments**, especially in the event of a pandemic. To facilitate this option, the governments and institutions that are funding or contributing to the development of drugs, vaccines and technologies against COVID-19 could require the recipients of funds to commit to **sharing their intellectual property rights on the grounds of extreme urgency**.

Sharing the benefits of a patent with affected populations does not oblige patent owners to give up their rights entirely. The commitment takes the form of a **social contract** by means of which the companies transfer their licences without geographical restrictions in exchange for the massive investment of public money by national governments to guarantee the production of safe and effective treatments at affordable prices for all. And this is not a utopian formula.

Ten years ago, UNITAID created the *Medicines Patent Pool* (MPP), an organisation that provides a framework for pharmaceutical companies to share their rights voluntarily. The MPP model has made possible the **manufacture of generic drugs that benefit tens of millions of people worldwide**. The use of this model, for example, has reduced the annual cost of treatment for HIV/AIDS to under $70 in Africa, as compared to $10,000 in Europe. The problem is that it took ten years to achieve this result.

Taking into account this prior experience, the European Union is supporting an intermediate initiative, the model being implemented by ACT-Accelerator through CEPI, GAVI and the WHO. This initiative combines push mechanisms, such as direct support to finance the expansion of manufacturing capacity, with financial incentives, such as an advance commitment by countries to purchase the end product at affordable prices. The aim is to incentivise companies to develop and produce the end product. The mission of this coordination mechanism, known as the COVID-19 Vaccine Global Access (COVAX) Facility, is **to ensure equitable access to the vaccine for all countries**.

At present, 54 countries are receiving grants from **GAVI, the Vaccine Alliance** to support immunisation campaigns targeting the 12 diseases that are responsible for most of the deaths that occur in children under five years of age. The challenge is not just to reduce the cost of immunisation in these countries, but also to bring the vaccine to all the low- and middle-income countries that would not qualify for these subsidies but for whom the high price of a COVID-19 vaccine would make it inaccessible ●

4. Conclusion and Recommendations

"The paradox of the race against COVID-19 is that the scientific challenges are perhaps the easiest obstacles to overcome. The most difficult and complex challenges arise once a vaccine has been developed: the manufacture of enough doses of the vaccine and their deployment prioritising the groups most in need while ensuring that all the world's countries can acquire the vaccine regardless of their resources."

The paradox of the race against COVID-19 is that the scientific challenges are perhaps the easiest obstacles to overcome. The most difficult and complex challenges arise once a vaccine has been developed: **the manufacture of enough doses of the vaccine and their deployment prioritising the groups most in need while ensuring that all the world's countries can acquire the vaccine** regardless of their resources. It is for these reasons that ISGlobal emphasises three basic recommendations during this process:

- **Public and private donors should ensure adequate funding for the development, production and deployment of one or more effective COVID-19 vaccines.** This funding effort should make use of all the traditional and innovative mechanisms that can serve to achieve these objectives.

- **The governance of the entire process should be based on the full and transparent participation of all the countries concerned,** but also take advantage of the opportunity offered by new forms of organisation such as ACT-Accelerator, an initiative that combines the efforts of experts, the industry and international bodies. A reformed and strengthened World Health Organisation can contribute to the vital leadership demanded by the challenge of immunisation.

- **In the management of intellectual property rights, the legitimate benefit of patent owners should be subordinated to public health objectives and the right of all countries and populations to an effective vaccine against COVID-19.** To this end, governments should make use of the flexibilities provided for in international agreements.

Even if a vaccine is approved within a year, it is unlikely that it will be available for deployment within that time frame. However, even without a vaccine, there is hope, as we have seen in the case of HIV. It will probably take much less time to identify antiviral **treatments** that already exist on the market which can help to reduce the severity of symptoms, speed up recovery, or decrease the transmissibility of the virus. Treatment, together with **good diagnostic and contact tracing tools**, can make a huge difference, even without a

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• La vacuna: el único camino de regreso a la vida anterior. El País. 31 May 2020.

• Access to COVID-19 Tools (act) Accelerator. WHO. 24 April 2020.

• Gavi and global health actors collaborate to accelerate COVID-19 technologies for all. 24 April 2020.

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