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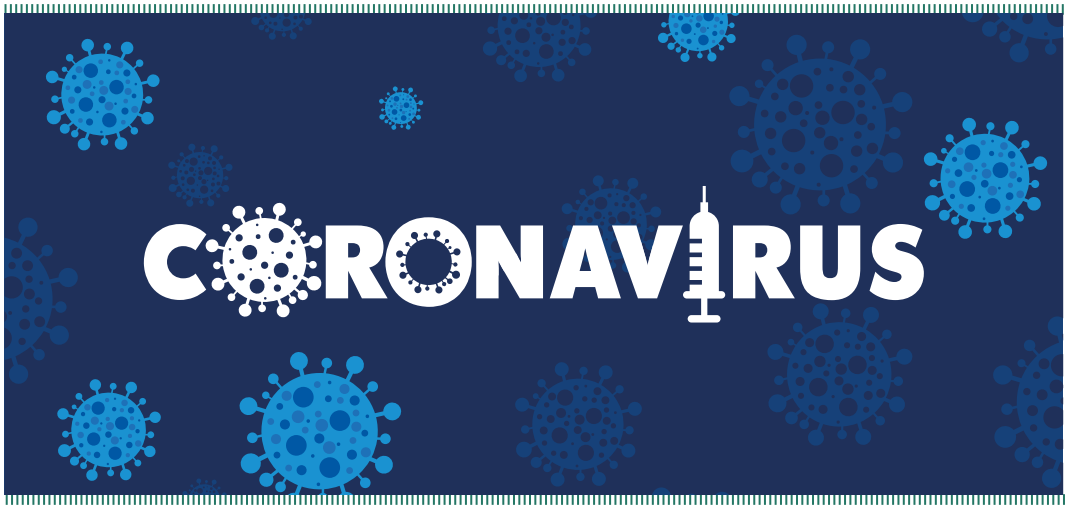
#COVID-19
#HEALTH

THE RACE FOR A COVID-19 VACCINE: A MAJOR CHALLENGE FOR EUROPE



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In the absence of an effective cure against COVID-19, only a safe and effective vaccine could put an end to the health crisis currently hitting the world, and Europe in particular. UN Secretary-General António Guterres even stated that only a vaccine can allow an eventual return to "normalcy". Such a vaccine could save millions of lives and would be a major prevention tool to increase collective immunity and avoid a cyclical return of the epidemic.

This global race is occurring today and is a battle for scientists from China, the USA, Europe and other areas. In order to finance research into a COVID-19 vaccine, the European Union held a major on-line pledging event, in cooperation with various governments and global partners, to appeal for donations, in the hope of collecting an initial amount of €7.5 billion, which will also be used for treatment and screening tests[1].

Charlie Weller, vaccine specialist at the Wellcome Trust, a global charity operating in the health sector, has called for stakeholders in the sector to prepare themselves "to execute the largest and fastest scale-up in vaccine manufacturing history". For Europeans, the challenge is not only finding a vaccine but manufacturing and distributing it as widely as possible. The stakes are multiple: health, economic, geopolitical.

1 ■ A race against time

The speed with which the new coronavirus was identified is one of the surprises of this epidemiological crisis. It took two years to isolate and describe the AIDS virus following the first case in Los Angeles in 1981, two months for the SARS virus, when the first sufferers were identified in Guangdong, China and then at the Metropole Hotel in Hong Kong in 2003, and only ten days for Chinese biologists to identify the sequence of this new coronavirus. On 29th January, the Institut Pasteur announced that it had sequenced the whole genome of the coronavirus known as "2019-NCoV".[2]

1. European Commission 2020. "Coronavirus global response: EU launches pledging effort", 24 April.
2. "Full sequencing was determined in three days", states Vincent Enouf, Deputy Director of the French National Reference Centre for viruses in *Le Figaro Magazine*, 6th March 2020.

1.1 ■ More than one hundred research projects

Across the globe, there is a large number of research projects to find a vaccine against COVID-19, the disease caused by the SARS-CoV-2 coronavirus. On 11th May, the WHO counted 110, eight of which (Chinese, American and European) have reached the clinical trial stage[3]. Around twenty pre-clinical tests are being conducted in various EU countries (Germany, France, Spain, Sweden, Italy, Belgium, Denmark, the Netherlands, Romania). Many of these projects are partnerships and involve several countries and organisations -research laboratories, start-ups, major pharmaceutical companies. In order to optimise the chances of success, researchers are working on several vaccine strategies.

1.2 ■ The first European clinical trials

1.2.1 Oxford University

A team of researchers from Oxford University in the UK launched clinical trials on a potential vaccine on 23rd April. The vaccine is based on a modified adenovirus vector causing infections in chimpanzees. The team has also secured the necessary capacity to manufacture one million doses of its candidate vaccine by September, if it proves effective and does not cause unacceptable side effects. The research work conducted by Oxford University, and that conducted by Imperial College London, is supported by the UK government.

1.2.2 BioNTech

On 22nd April, the German federal authority in charge of vaccine certification green-lighted clinical trials for an experimental vaccine developed jointly by German biotechnology company BioNTech, US pharmaceutical giant Pfizer and the Chinese laboratory Shanghai Fosun Pharmaceutical. BioNTech is competing against fellow German company CureVac[4] and with US biotechnology company Moderna Therapeutics to develop an unprecedented process which involves injecting humans with RNA (part of the genetic make-up of the SARS-CoV-2 virus)[5]. Moderna has launched clinical trials; CureVac states that it should be able to start trials by June.

1.3 ■ The examples of Pasteur and Sanofi

Following the international call for proposals launched on 30th January, the international coalition CEPI[6] (Coalition for Epidemic Preparedness Innovations) announced on 19th March that it had allocated €4.3 million to the first development phases of a SARS-CoV-2 vaccine resulting from research by the Institut Pasteur as part of a consortium with Austrian company Themis BioScience and the US University of Pittsburgh/ Center for Vaccine Research (CVR). The first clinical trials are set to begin in September 2020. This project is based on the use of the measles vaccine as a vehicle for this candidate vaccine[7].

French company Sanofi and British company GlaxoSmithKline (GSK) announced on 14th April a partnership for the development of a COVID-19 vaccine[8]. The two laboratories wish to tap into their respective technologies, in particular the S-protein virus antigen developed by the French group. Sanofi and GlaxoSmithKline plan to launch phase I clinical trials in the second semester of 2020 and hope to be able to make the vaccine available by the second semester of 2021. They have received funding from the US Biomedical Advanced Research and Development Authority (BARDA).

3. WHO 2020. "Draft landscape of COVID 19 candidates vaccines", 11th May.
4. In order to keep CureVac within the European system, the Commission proposed as early as 16th March financial assistance of up to €80 million, in the form of an EU guarantee that would cover a loan from the EIB for an identical amount, under the "infectious diseases" section of the InnovFin financing mechanism within the Horizon 2020 programme. The EIB has agreed assistance of €75 million.
5. These molecules acts as intermediaries that instruct cells to produce antigen proteins, which allow the immune system to develop defences against future coronavirus infections.
6. Three years ago, the Bill and Melinda Gates Foundation, the Wellcome Trust and various governments launched the CEPI international coalition with a view to speeding up the vaccine testing process and to financing new and faster immunisation methods (https://cepi.net). Despite new contributions in recent weeks, the Coalition believes that an additional amount of at least $2 billion will be necessary for the development of three candidate vaccines in the next 18 months, excluding manufacturing and distribution.
7. The Institut Pasteur is developing three vaccine strategies: two based on the use of attenuated viruses – the virus used in the measles vaccine, an anti-virus of the HIV family – ; one based on DNA vaccination.
8. Sanofi and GSK have decided to coordinate their efforts. Sanofi, which has large production capacity for flu vaccines, will use this platform to produce the antigen, one of the vaccine's active ingredients, while GSK will produce the adjuvant, which means that a very large quantity of vaccines will be possible.

2 ■ A long and risky process

Developing a vaccine usually takes many years and significant financial resources[9]. It takes on average a year and a half to produce a vaccine that can be used in humans and another year to complete the last clinical trial phase. Given the severity of the current pandemic, time pressures and the economic crisis, work may be accelerated. Yet, while the most optimistic believe that it may be possible to have a vaccine ready by the end of 2020, 2021 appears a more realistic timescale. A company will never take the risk of marketing a vaccine which does not meet all the security standards.

2.1 ■ Several research phases

Candidate vaccines are first of all tested in laboratories on cells and animals (pre-clinical testing).

Conducted by doctors or hospital teams, clinical trials are subsequently rolled out in several phases:

- Phase 1: Trials are conducted mainly on a limited number of healthy subjects, under strict medical supervision, in order to determine the **safety** of the candidate vaccine in humans.

- Phases 2 and 3: Trials are conducted on increasingly larger patient populations. The aim is to test the **efficacy** of the product and to determine the optimal dose (dosage) with a view to a possible marketing authorisation granted by health authorities.

- Phase 4: Trials continue throughout the marketing phase. They aim to identify any rare adverse effects which were not detected during the previous phases (**pharmacovigilance**) and to specify the conditions of use for certain at-risk patient groups.

2.2 ■ A high financial cost

This health crisis highlights the weaknesses of European research systems. "Even if we have consortia of researchers, a common drive to take action, a series of European projects financed by the Commission, we in Europe are still falling very short of the amounts the USA is investing in vaccine research", deplores MEP (Renew Europe) Véronique Trillet-Lenoir[10]. **Even though Europe has significant fire power in terms of technology and expertise, it is suffering from the significant hurdle of lower financial resources allocated to research than those of its major partners.**

Yet, for private companies, the development of a vaccine is considered extremely risky, long and expensive. Colossal sums of money are necessary, given that the probability of success is low and that a vaccine may be deprived of an outlet if the pandemic stops suddenly, as was the case with the SARS virus in 2003. The development cost of a vaccine is usually between €500 million and €2 billion according to best-case scenarios, not including pre-clinical testing[11].

2.3 ■ The gamble of manufacturing

The level of technical complexity and safety required in this field is so great that only a handful of companies in the world have the expertise, resources and infrastructure required to manufacture vaccines. While the pharmaceutical industry is concentrated around a few major global players such as Pfizer, Novartis, Roche, Sanofi, Johnson & Johnson, Merck or GSK[12], Europe has a strong position in this area. According to data disclosed by Vaccines Europe, **around three quarters of global vaccines are manufactured in Europe** (including in Switzerland and the United Kingdom).

Given the number of doses which will be necessary to combat COVID-19, it is important to start to plan requirements, decide what will be manufactured, how and for whom, by identifying where possible priority groups - key workers, at-risk populations, the elderly[13]. Major pharmaceutical firms will need clear directives so that they can

9. "Making a vaccine takes time", reminded Marie-Paule Kieny, research director at INSERM in an interview with *Le Figaro*.
10. Interview with the author on 29th April 2020.
11. In the case of COVID-19, the Bruegel think tank suggests a provision for additional public funding, which may reach €3 billion, so that there are enough candidate vaccines to minimise the risks of failure.
12. According to a classification table drawn up by Leem (the French industry association which represents drug companies operating in France), the top ten global pharmaceutical companies in 2018 were: Novartis (Switzerland); Johnson & Johnson (USA); Pfizer (USA); Roche (Switzerland); Sanofi (France); GlaxoSmithKline (UK); Merck & Co (USA); AbbVie (USA); Lilly (USA) and Gilead Science (USA).
13. In an opinion piece in *Le Monde*, American philantropist Bill Gates insists on the importance of international consultation and the need to leave egos at the door if we are to beat the pandemic.

organise themselves and be able to supply sufficient quantities of vaccines on a very large scale and at the right time. Even for the most common vaccines (flu, chicken pox), governments often do not give sufficient information on medium-term requirements.

Usually, a company does not invest in the massive production of a vaccine until clinical trials are completed. However, given the stakes of the current pandemic, **some companies, in particular American and Chinese ones, are ready to launch production before the end of clinical trials in order to be the first to market the vaccine** when one is ready. This assumption of risk may pay off, but this implies having significant financial means.

2.4 ■ Support from the European Union

The European Commission has allocated €5.7 million to two vaccine research projects: OPENCORONA, developed by the Swedish Karolinka Institutet with seven partners from Sweden, Germany and Italy, and Prevent-nCov, developed by the Danish Kobenhavns Universitet with seven partners from Denmark, Germany and the Netherlands[14].

The EU has also leveraged public and private funding, which could reach €90 million, through the Innovative Medicines Initiative. It is also contributing €20 million to the Coalition for Epidemic Preparedness Innovations (CEPI). Lastly, the European and Developing Countries Clinical Trials Partnership (EDCTP) is financing three calls under the Horizon 2020 programme. The amount could reach €28 million. The aim here is to support research into SARS-CoV-2 and to step up research capacities in sub-Saharan Africa.

In addition, the Commission, in cooperation with several partners, launched on 20th April a European COVID-19 data platform (which is part of the ERAvsCorona action plan[15]) with a view to collecting and sharing available data as quickly as possible. Researchers can store and share data sets on the platform (DNA sequences, protein structures, data from pre-clinical research and clinical trials, epidemiological data)[16].

3 ■ Multiple challenges for Europeans

The USA hopes to win the vaccine war and is ready to put all its strength into the battle. The German government had to intervene in March to stop *in extremis* attempts, steered by the White House, to acquire the pharmaceutical company CureVac, which had announced promising initial trials.

China, the place of origin of the epidemic, is also on the front line: research there has received considerable state support and is in full swing, with four projects already at the clinical trials phase, in particular the project conducted by the laboratory Sinovac BioTech, which was the first in 2009 to market a vaccine against the H1N1 swine flu.

Europeans, meanwhile, enjoy quality research, although their teams often work under relatively complex consortium structures. If they want to win, they will not only have to discover the first vaccine likely to be marketed on a large scale, but must also be able to produce it at least partially within the EU. Such an achievement would structure the narrative of a genuine European success story.

3.1 ■ An economic challenge

For the team who will find the vaccine, as for the company which will manufacture it, there will be enormous spin-offs in terms of revenue and reputation. **Discovering a COVID-19 vaccine would empower the European research sector in the country or countries concerned, which would extend to other issues.** Unlike development costs, which account for most added value, manufacturing costs are more limited; companies can therefore hope to achieve relatively high profit margins.

For a vaccine such as the one intended to combat COVID-19, the main, if not exclusive, buyers will most certainly be governments. The issue will therefore be to set a price that is sufficiently affordable to make the vaccine accessible to the greatest number of people and sufficiently high so that companies are not discouraged from investing in production. In order to avoid mono-

14. Another call for proposals concerning the development of vaccines has been launched by the European Commission. A working group has also been monitoring the entire sector of vaccines, treatments and tests since 7th April.
15. On 7th April, the ministers for research and innovation in the 27 EU Member States agreed on ten priority actions based on close coordination, cooperation, data-sharing and joint financing efforts between the Commission and the Member States.
16. The Commission is drawing up a strategic communication on clinical trials in the hope of having a European network which can identify the most promising companies and see how production can be scaled up quickly when the time comes.

poly situations, some countries could use the compulsory licence, a legal measure that allows countries to suspend patent exclusivity on a product, thereby enabling them to purchase it or produce it freely[17].

3.2 ■ A sovereignty challenge

Facing such a pandemic, the first challenge will be to have enough doses of vaccine, which will mean a race to become the highest and best bidder when the time comes. The countries that will have produced the vaccine first will tend to favour their own citizens and enforce their own conditions. **If it loses the battle, Europe could find itself in a position of weakness in relation to the USA or China.** Conversely, if a vaccine is produced by Europe and in Europe, we could imagine that Europe would be given priority while planning distribution to third countries.

Not all EU Member States are in the same boat. Some, such as Germany and France, have a great degree of latitude in the international arena, both to produce a vaccine and to purchase one, while others do not have the sufficient critical mass or scientific capacities. Europeans will therefore have to act together, both to provide mutual assistance and to be in a stronger position on an international level.

3.3 ■ A health and geopolitical challenge

Europeans will have a part to play to ensure that doses are distributed fairly and that they are not in the hands of the richest countries, resulting in "vaccine nationalism"[18]. Poorer countries will most likely be better treated if there is an alliance between Europe, China and the USA than if each one plays its own hand (*cf.* 4.3). It is in the interest of all: the only way to stop the pandemic is to have the greatest number of people vaccinated across the globe.

On 24th April, the WHO and a first group of global healthcare sector partners launched a global cooperation initiative with a view to accelerating the development and production of new key medical technologies to combat COVID-19. This group includes the Bill and Melinda Gates Foundation (BMGF), the Coalition for Epidemic Preparedness Innovations (CEPI), GAVI (global vaccine alliance), the Global Fund, UNITAID, the Wellcome Trust and the World Bank. Together, they committed to a shared goal of fair and universal access to innovative tools to combat the COVID-19 pandemic.

A vaccine produced by the world as a whole could be considered to be a "unique global public good of the 21st century", available, accessible and affordable for all[19]. The organisers of the pledging event on 4th May hope that the funds collected will kick off global cooperation between scientists, regulators, industry players, governments, international organisations, foundations and healthcare professionals.

4 ■ Pathways for the future

4.1 ■ Strengthening research and production capacities

One avenue would be to step up public funding allocated to the discovery and production of a vaccine: new initiatives could emerge if they enjoyed a financial guarantee, there would be an advantage in sharing what is done by the different parties. The battle for a vaccine may be long, ongoing and may end with several winners. Working together would enable States to enforce conditions in terms of prices and fair distribution.

4.2 ■ Coordinated action on a European level

Excluding the research programmes co-financed by the EU budget, **there is nothing on a European level to create vaccines together, no standards or legal instruments**. The added value of a European strategy for a vaccine against respiratory pandemics would be very clear in terms of critical mass, bargaining power and geopolitical importance. There have been past alliances between some Member States to obtain favourable rates, which could point to broader agreements.

17. Ellen't Hoen and Achal Prabhala propose to establish a pooling mechanism whereby no technology related to COVID-19 may be subject to a monopoly and in which innovation would be financed by public funds and stimulated by international cooperation.
18. "it is just unacceptable that there is not fair access to a successful vaccine across the world's population", Jane Halton, Chair of CEPI, explained to *The Guardia*n. During the H1N1 crisis, wealthy countries negotiated a high number of orders in advance, to the detriment of poor countries. Jane Halton talks about "vaccine nationalism": one billion inhabitants are considered vulnerable across the world.
19. 2020. "Von der Leyen, Michel, Macron, Merkel, Conte, Solberg détaillent le Téléthon mondial contre le Covid", *Le Journal du dimanche*, 1st May (in French).

Conducting genuine action across the twenty-seven Member States requires political drive. It also involves overcoming the natural reflexes of many governments, which are often lacking transparency regarding their purchasing policy and jealous of their expertise, particularly when they have their own pharmaceutical industry.

This crisis could be an opportunity to **establish a new and inclusive form of European governance based on an ecosystem of vaccines**, which would mean that various issues such as research, distribution, pricing and distribution can be tackled together. For the EU, to be able to vaccinate all its citizens is a strategic challenge.

4.3 ■ Establishing a global governance for vaccines

Real global governance, including producer and non-producer countries, should be established to organise the production, marketing and distribution of vaccines of vital importance to the world's population.

Europe will be in a better position to fight for poor countries' access to the vaccine if it enters into a prior agreement with the USA and China in the event of either of these nations producing one. The EU-27 will want to ensure that they can offer their citizens the necessary vaccines, without being dependent on the good will of these two powers, before ensuring that all other countries have a supply.

One solution could be to strengthen the GAVI Alliance, a structure for the development and production of vaccines which assists low-revenue nations to access essential vaccination campaigns[20].

Conclusions ■

In this race for a COVID-19 vaccine, a victory for Europe would be to establish a new form of governance and to obtain a high level of cooperation between companies, laboratories and governments to develop a vaccine. For the marketing and international negotiation of the future vaccine, success would also involve demonstrating that the critical mass of around 500 million citizens makes a difference.

The COVID-19-related health crisis could convince the most reluctant people of the utility of vaccines, many of whom are located in France, as vaccines remain the most important, most effective and most inexpensive public health instrument in our history.

20. In order to leverage more resources and coordinate efforts against COVID-19, the President of the Commission, Ursula von der Leyen, could propose a cooperation framework made up of three public-private partnerships, each bringing together scientists, pharmaceutical industries and regulators; the CEPI and the GAVI Alliance would be responsible for drawing up the group's vaccine programme.

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