Update on COVID-19 vaccine development

THE LATEST ON THE COVID-19 GLOBAL SITUATION & VACCINE DEVELOPMENT
Overview

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Current global situation

AS OF 20 DECEMBER 2020; 10H CEST

• **> 75 million cases**
  - 5 countries with highest cumulative number of cases
    - United States of America
    - India
    - Brazil
    - Russian Federation
    - France

• **> 1,68 million deaths**
  - 5 countries with highest cumulative number of deaths
    - United States of America
    - Brazil
    - India
    - Mexico
    - Italy
Current global situation

CASES REPORTED TO WHO AS OF 20 DECEMBER 2020, 10:00 CEST

* Data are incomplete for the current week. Cases depicted by bars; deaths depicted by line
COVID-19 cases reported in the last 7 days
Per million population

FROM 13 DECEMBER 2020, 10:00AM CEST to 20 DECEMBER 2020, 10:00 AM CEST
COVID-19 deaths reported in the last 7 days
Per million population

FROM 13 DECEMBER 2020, 10:00AM CEST to 20 DECEMBER 2020, 10:00 AM CEST
Why do we need vaccines for COVID-19?

- **Vaccines can prevent infectious diseases.** Vaccines do prevent measles, polio, hepatitis B, influenza and many others.

- When most people in a community are protected by vaccination, the ability of the pathogen to spread is limited. This is called ‘herd’ or ‘indirect’ or ‘population’ immunity.

- When many people have immunity, this also indirectly protects people who cannot be vaccinated, such as those who have compromised immune systems.
ABOUT VACCINES

How COVID-19 vaccines work

- **Vaccines greatly reduce the risk of infection** by training the immune system to recognize and fight pathogens such as viruses or bacteria.

- Most research on COVID-19 vaccines involves generating responses to all or part of the *spike protein* that is unique to the virus that causes COVID-19. When a person receives the vaccine, it will trigger an immune response.

- If the person is infected by the virus later on, the immune system recognizes the virus and, because it is already prepared to attack the virus, protects the person from COVID-19.
How safe are the COVID-19 vaccines?

- The safety requirements for COVID-19 vaccines are the same as for any other vaccine and will not be lowered in the context of the pandemic
- Safety trials begin in the lab, with tests and research on cells and animals first, before moving on to human studies
- The principle is to start small and only move to the next stage of testing if there are no safety concerns
- Clinical trials are evaluating COVID-19 vaccines in tens of thousands of study participants to generate the scientific data and other information needed to determine safety and effectiveness
- These clinical trials are being conducted by manufacturers according to rigorous standards
- The COVID-19 vaccines are tested in a broad population of people – not only young, physically fit volunteers, but also older people and people with underlying health conditions
- After deployment, the vaccines will continue to be carefully monitored for safety and effectiveness

Monitoring of adverse events following immunization

- Monitoring of adverse events following immunization (AEFI) is an essential strategy for ensuring the safety of vaccines.

- An AEFI is any untoward medical occurrence which follows immunization. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease but does not necessarily have a causal relationship with the usage of the vaccine.

- A serious AEFI is an event that results in death, hospitalization or prolongation of an existing hospitalization, persistent or significant disability or incapacity, congenital anomaly/birth defect or is life-threatening.

- At the time of vaccine introduction, all countries should have an AEFI surveillance system in place as described in the Global Manual on Surveillance of AEFI.

- All AEFIs should be reported using the standard COVID-19 AEFI reporting form using the fastest means possible.

Source:
2. https://www.who.int/vaccine_safety/committee/Module_AEFI.pdf?ua=1
What is an emergency use authorization in the context of COVID-19 vaccines?

• An emergency use authorization is a mechanism to facilitate the availability and use of vaccines, during public health emergencies, such as the current COVID-19 pandemic.

• In an emergency, like a pandemic, vaccines may be temporarily approved for use under an emergency use authorization as it may not be possible to have all the evidence that regulators would usually have before full approval (for example adverse events in specific populations that were not covered by clinical trials or those that occur rarely).

Source: https://www.fda.gov/vaccines-blood-biologics/vaccines/emergency-use-authorization-vaccines-explained
Vaccine benefits must outweigh the potential risks

Emergency use authorization

• For an emergency use authorization to be issued for a vaccine, it must be determined that the benefits outweigh the known and potential risks of the vaccine

• An emergency use authorization considers all safety data accumulated from phase 1 and 2 studies. In addition, at least half of vaccine recipients in phase 3 clinical trials should have at least 2 months of follow-up after completion of the full vaccination regimen

• Vaccine manufacturers must actively follow-up on safety, including deaths and serious adverse events, among individuals who receive the vaccine under an emergency use authorization

Source: https://www.fda.gov/vaccines-blood-biologics/vaccines/emergency-use-authorization-vaccines-explained
What is done to fast-track vaccine development in a public health emergency

• Continuous dialogue between developers and regulatory experts and early **scientific advice** helps speed up vaccine development. Advising companies on regulatory requirements helps ensure that standards of **safety** and **efficacy** are embedded early in the process and are not compromised by fast-track development.

• Resource mobilization for COVID-19 vaccines is done simultaneously which allows for accelerated development and manufacturing of vaccines.

• Companies may use various approaches to reduce **development timelines**, such as:
  - mobilize more staff to analyze results from studies more quickly and map out next steps in terms of resources, funding and regulatory strategy
  - combine clinical trial phases or conducting some studies in parallel where safe to do so

• Companies are expanding **manufacturing capacity** and large-scale production, to facilitate vaccine deployment without delay once approved.

Steps in vaccine development
Actions taken to ensure a new vaccine is safe and works well

- **Pre-clinical studies**
  Vaccine is tested in animal studies for efficacy and safety, including challenge studies

- **Phase I clinical trial**
  Small groups of healthy adult volunteers receive the vaccine to test for safety

- **Phase II clinical trial**
  Vaccine is given to a larger group of people who have characteristics (such as age and physical health) similar to those for whom the new vaccine is intended

- **Phase III clinical trial**
  Vaccine is given to thousands of people and tested for efficacy and safety

- **Phase IV post marketing surveillance**
  Ongoing studies after the vaccine is approved and licensed, to monitor adverse events and to study long-term effects of the vaccine in the population

- **Human challenge studies**
  Studies in which a vaccine is given followed by the pathogen against which the vaccine is designed to protect. Such trials are uncommon in people as they present considerable ethical challenges
COVID-19 vaccine accelerated development

- Normal vaccine development performs each step in sequence
- To accelerate COVID-19 vaccine development, **steps are done in parallel**
- Accelerated development increases the financial risk for manufacturers

- All usual safety and efficacy monitoring mechanisms remain in place; such as adverse event surveillance, safety data monitoring & long-term follow-up
- **Phase IV post-marketing surveillance** for side effects is critical and essential
COVID-19 vaccine candidates in Phase III trials

- As of 16 December 2020 there are 56 COVID-19 candidate vaccines in clinical evaluation of which 13 are in Phase III trials
- There are another 166 candidate vaccines in preclinical evaluation
- Phase III trials usually require 30,000 or more participants
- All top candidate vaccines will be delivered through intra-muscular injection
- Most are designed for a two-dose schedule (exceptions with a * in table are single dose)

<table>
<thead>
<tr>
<th>13 CANDIDATE VACCINES IN PHASE III CLINICAL EVALUATION</th>
<th>VACCINE PLATFORM</th>
<th>LOCATION OF PHASE III STUDIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinovac</td>
<td>Inactivated virus</td>
<td>Brazil</td>
</tr>
<tr>
<td>Wuhan Institute of Biological Products / Sinopharm</td>
<td>Inactivated virus</td>
<td>United Arab Emirates</td>
</tr>
<tr>
<td>Beijing Institute of Biological Products / Sinopharm</td>
<td>Inactivated virus</td>
<td>China</td>
</tr>
<tr>
<td>Bharat Biotech</td>
<td>Inactivated virus</td>
<td>India</td>
</tr>
<tr>
<td>University of Oxford / AstraZeneca</td>
<td>Viral vector</td>
<td>USA</td>
</tr>
<tr>
<td>CanSino Biological Inc. / Beijing Institute of Biotechnology</td>
<td>Viral vector *</td>
<td>Pakistan</td>
</tr>
<tr>
<td>Gamaleya Research Institute</td>
<td>Viral vector</td>
<td>Russia</td>
</tr>
<tr>
<td>Janssen Pharmaceutical Companies</td>
<td>Viral vector</td>
<td>USA, Brazil, Colombia, Peru, Mexico, Philippines, South Africa</td>
</tr>
<tr>
<td>Novavax</td>
<td>Protein subunit</td>
<td>The United Kingdom</td>
</tr>
<tr>
<td>Anhui Zhifei Longcom Biopharma/ Institute of Microbiology, Chinese Academy of Sciences</td>
<td>Protein subunit</td>
<td>China</td>
</tr>
<tr>
<td>Moderna / NIAID</td>
<td>RNA</td>
<td>USA</td>
</tr>
<tr>
<td>BioNTech / Fosun Pharma / Pfizer</td>
<td>RNA</td>
<td>USA, Argentina, Brazil</td>
</tr>
<tr>
<td>Medicago Inc</td>
<td>VLP</td>
<td>Canada</td>
</tr>
</tbody>
</table>

Source: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

* Single dose schedule
Four COVID-19 vaccines have submitted data to regulatory authorities for emergency authority use

<table>
<thead>
<tr>
<th>Company</th>
<th>Type</th>
<th>Doses</th>
<th>How effective</th>
<th>Storage</th>
<th>Emergency authority use granted</th>
<th>Emergency authority use being reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxford Uni-AstraZeneca</td>
<td>Viral vector (adenovirus modified to carry the spike protein)</td>
<td>x2</td>
<td>62-90%</td>
<td>Regular fridge temperature</td>
<td>India</td>
<td></td>
</tr>
<tr>
<td>Moderna</td>
<td>mRNA (part of virus genetic code)</td>
<td>x2</td>
<td>95%</td>
<td>-20°C up to 6 months</td>
<td>USA</td>
<td>European Medicines Agency (EMA)</td>
</tr>
<tr>
<td>Pfizer-BioNTech</td>
<td>mRNA</td>
<td>x2</td>
<td>95%</td>
<td>-70°C</td>
<td>Canada, UK, EMA, Switzerland, USA</td>
<td>India</td>
</tr>
<tr>
<td>Gamaleya (Sputnik V)</td>
<td>Viral vector</td>
<td>x2</td>
<td>92%</td>
<td>Regular fridge temperature</td>
<td>Russia</td>
<td></td>
</tr>
</tbody>
</table>

Sources:
How the mRNA vaccines work
Pfizer-BioNTech and Moderna are mRNA vaccines

• The traditional methods of vaccine development introduce the body to either an inactivated or weakened form of a virus or to one of its viral proteins

• Instead, **mRNA vaccines inject nucleic acid coding for the antigen**

• The development of mRNA vaccines is faster as it bypasses the more laborious tasks of inactivating viruses or isolating proteins

Source: [https://www.nationalgeographic.com/science/2020/05/moderna-coronavirus-vaccine-how-it-works-cvd/](https://www.nationalgeographic.com/science/2020/05/moderna-coronavirus-vaccine-how-it-works-cvd/)
Understanding mRNA COVID-19 vaccines

mRNA vaccines do not affect or interact with our DNA in any way

• The cell breaks down and gets rid of the mRNA soon after it is finished using the instructions to make a protein

• mRNA vaccines use a new technology. However, mRNA vaccines have been studied before for flu, Zika, rabies, and cytomegalovirus

• Future mRNA vaccine technology may allow for one vaccine to provide protection for multiple diseases, thus decreasing the number of shots needed for protection against common vaccine-preventable diseases.

• Beyond vaccines, cancer research has used mRNA to trigger the immune system to target specific cancer cells

Source:
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/mrna.html#text=COVID%2D19%20mRNA%20vaccines%20are%20protein%20on%20its%20surface
Why reported results from the Oxford Uni-AstraZeneca COVID-19 vaccines clinical trial differ

The Oxford Uni-AstraZeneca COVID-19 vaccine trial included two groups.

In one group, patients were given a vaccine which consisted of a **smaller initial dose followed by a larger booster dose one month later**. Data analysis found that the vaccine was about **90% effective** at preventing COVID-19 in this group.

In the second group, patients were given the same dose in both instances, producing a lower efficacy rate of **62%**.

When combining both groups efficacy was **70%**.

It is not yet clear why a smaller initial dose performs better. But it has been suggested it could be because a larger initial dose prompts the body to produce antibodies against the vaccine itself.

Source: [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32623-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32623-4/fulltext)
Why are there so many COVID-19 vaccines in development?

- There are many different COVID-19 vaccines in development using different technologies because it is not yet known which ones will be effective and safe.
- Based on experience, roughly 7% of vaccines in preclinical studies succeed. Candidates that reach clinical trials have about a 20% chance of succeeding.
- Different vaccine types may be needed for different population groups.
- For example, some vaccines may work in older persons and some may not, as the immune system weakens with older age.
- Several vaccines are needed to allow countries with as much vaccine as possible to increase the supply.
- Not everyone will be able to be vaccinated right away because of limited supply. It is important that the initial supplies of vaccine are given to people in a fair, ethical, and transparent way.
- WHO recommends prioritization based on the WHO SAGE Prioritization Roadmap.

Source:
The difference between efficacy and effectiveness of COVID-19 vaccines

- **Efficacy** is the performance of a treatment under ideal and controlled circumstances such as a clinical trial, and **effectiveness** is performance under real-world conditions.

- **Monitoring of vaccines does not stop after they are approved for use.** When the vaccine is deployed, data will continue to be collected to study how well it works over time for all vaccinated people to report on **effectiveness**.

- It may be several years before we know what the overall **effectiveness** of the vaccines will be in preventing COVID-19 symptoms, severe disease or deaths.

Source:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3912314/#:%7E:text=Efficacy%20can%20be%20defined%20as%2C%20'real%2Dworld%20conditions.
WHO VACCINES & IMMUNIZATION-RELATED COMMITMENTS

Working together to deliver vaccine to all countries

COVAX

• The COVAX Facility is an unprecedented global effort to ensure that whatever vaccine proves safe and effective, each country in the world has equitable access to it as quickly as possible.

• Coordinated by WHO, GAVI and the Coalition for Epidemic Preparedness Innovations (CEPI), COVAX acts as a platform that supports the research, development and manufacturing of a wide range of COVID-19 vaccine candidates, and negotiate their pricing.

• All participating countries, regardless of income levels, will have equal access to these vaccines once they are developed. The aim is to have 2 billion vaccine doses available by the end of 2021.

• 189 countries and economies have signed up, including self-financing ones and 92 lower-income countries which are eligible for financial support through GAVI.

• Over US$ 2 billion has been raised to support equitable access to COVID-19 vaccines with an additional US$ 5 billion needed in 2021.

Sources:
https://www.who.int/initiatives/act-accelerator/covax
https://www.gavi.org/vaccineswork/covax-explained
COVID-19 vaccine development mobilizes resources simultaneously

- **Through COVAX**, CEPI has raised money to support the research and development of a diverse portfolio of COVID-19 vaccine candidates

Sources:
Can we all go back to our normal life once vaccinated?

- The Pfizer-BioNTech and Moderna vaccine trials show that COVID-19 vaccines are effective in preventing severe disease.

- However, neither the Pfizer-BioNTech nor the Moderna vaccine trials tested whether the vaccines prevent people from being infected with the virus, that means that it’s not clear whether vaccinated people could still transmit COVID-19 to others.

- We don’t know yet the duration of immunity conferred by the vaccines.

- In addition, it will take time to vaccinate everyone. Until that happens and until it’s clear how well the vaccines prevent transmission, other public health and social measures such as physical distancing and wearing of masks will be needed.

Sources:
MONITORING SOCIAL MEDIA

ALLEVIATING VACCINE FEARS

• Much of the discussion surrounding potential COVID-19 vaccines came from the US, where three former Presidents committed to getting a COVID-19 vaccine on camera, to alleviate the fears of citizens concerned about getting the vaccine

• Commenters were positive about this example of leadership, and many stated it would make them feel more confident about taking the vaccine

ENGAGEMENT INITIAL VACCINATIONS

• The United Kingdom began vaccinations against COVID-19, inoculating older and vulnerable populations with the Pfizer/BioNTech vaccine

• Comments from users doubting the safety and efficacy of the vaccine demonstrated knowledge gaps about the vaccine testing and development process, and several posts incorrectly stating that the vaccine had not passed clinical trials received high engagement

Most discussed topics online on COVID-19 vaccines

12 NOVEMBER to 09 DECEMBER 2020

GLOBAL INDEXED GOOGLE SEARCHES OF COVID-19 VACCINES

12 Nov – 09 Dec 2020

Top countries discussing vaccines

03 Dec – 09 Dec 2020

Vaccines

+92%
COVID-19 vaccination training for health workers
OpenWHO

- This course provides general information on COVID-19 and specific information on:
  - **Storage, handling and administration of the vaccine**, recording and monitoring including for adverse events following immunization (AEFI)
  - **Communication** (acceptance and demand)
- This course is primarily for frontline health workers who will be vaccinators and priority recipients

Sources:
https://openwho.org/courses/covid-19-vaccination-healthworkers-en
Resources on COVID-19 vaccine development

<table>
<thead>
<tr>
<th>Resources</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WHO Target Product Profile for COVID-19 vaccine</strong></td>
<td>This Target Product Profile (TPP) describes the preferred and minimally acceptable profiles for human vaccines for long term protection of persons at high ongoing risk of COVID-19, such as health workers, and for reactive use in outbreak settings with rapid onset of immunity.</td>
</tr>
<tr>
<td><strong>Vaccine landscape</strong></td>
<td>Landscape documents prepared by the WHO for information purposes concerning the 2019-2020 global development of new COVID-19 vaccines.</td>
</tr>
<tr>
<td><strong>Access to COVID Tools (ACT) Accelerator</strong></td>
<td>The vaccines pillar of the ACT Accelerator, convened is speeding up the search for an effective vaccine for all countries.</td>
</tr>
<tr>
<td><strong>COVAX: Working for global equitable access to COVID-19 vaccines</strong></td>
<td>WHO</td>
</tr>
<tr>
<td><strong>Covax explained</strong></td>
<td>GAVI</td>
</tr>
<tr>
<td><strong>COVAX: CEPI’s response to COVID-19</strong></td>
<td>CEPI</td>
</tr>
<tr>
<td><strong>Q&amp;A: Coronavirus disease (COVID-19) Vaccines</strong></td>
<td>A Q&amp;A including answers to questions on vaccine development, distribution and safety</td>
</tr>
<tr>
<td><strong>WHO Guidance on ethics of vaccine allocation</strong></td>
<td>This policy brief answers a number of questions about the ethics of setting priorities for the allocation of resources during times of scarcity. Such decisions may include access to hospitals, ventilators, vaccines and medicines</td>
</tr>
<tr>
<td><strong>How do vaccines work?</strong></td>
<td>This article is part one in a series of explainers on vaccine development and distribution. This article focuses on how vaccines work to protect our bodies from disease-carrying germs</td>
</tr>
<tr>
<td><strong>How are vaccines developed?</strong></td>
<td>This article is part two in a series of explainers on vaccine development and distribution. This article focuses on the ingredients in a vaccine and the three clinical trial phases</td>
</tr>
<tr>
<td><strong>Manufacturing, safety &amp; quality control of vaccines</strong></td>
<td>This document is part three in a series of explainers on vaccine development and distribution</td>
</tr>
<tr>
<td><strong>WHO SAGE values framework</strong></td>
<td>For the allocation and prioritization of COVID-19 vaccination</td>
</tr>
<tr>
<td><strong>WHO SAGE prioritization roadmap</strong></td>
<td>An approach to help inform deliberation around the range of recommendations that may be appropriate under different epidemiologic and vaccine supply conditions</td>
</tr>
</tbody>
</table>
How to protect ourselves & others
9 important COVID-19 prevention measures

01 Stay home and self-isolate if you feel unwell, even with mild symptoms

02 Clean hands frequently with soap & water for 40 seconds or with alcohol-based hand rub

03 Cover your nose and mouth with a disposable tissue or flexed elbow when you cough or sneeze

04 Avoid touching your eyes, nose and mouth

05 Maintain a minimum physical distance of at least 1 metre from others

06 Stay away from crowds and avoid poorly ventilated indoor spaces

07 Use a fabric mask where physical distancing of at least 1 metre is not possible

08 Use a medical / surgical mask if you may be at higher risk (age, medical conditions)

09 Regularly clean & disinfect frequently touched surfaces