PAHO/WHO

Update on COVID–19 Vaccines Development

October 15, 2020

Pan American Health Organization
World Health Organization
Americas

PAHO

PAHO/WHO

Context

As the COVID-19 pandemic continues to affect countries around the world the number of cases and deaths are increasing significantly.

While rigorous testing, contact tracing, quarantine, isolation and evidence-based public health measure help to control the spread of COVID-19; the development and implementation of a vaccine will contribute significantly to reduce the threat.

The development of a novel vaccine is a complex and lengthy process that on average takes 10 years.

Given the current COVID-19 pandemic, institutions, commercial developers, and researchers around the world are working at an unprecedented speed.

As of 02 October 2020, they were 42 candidate vaccines in clinical evaluation in humans and 151 candidate vaccines in the preclinical phase

Pan American Health Organization
World Health Organization
Regional Office for the Americas
PAHO

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 people who have characteristics (such as age and physical health) similar to those for whom the new vaccine is intended

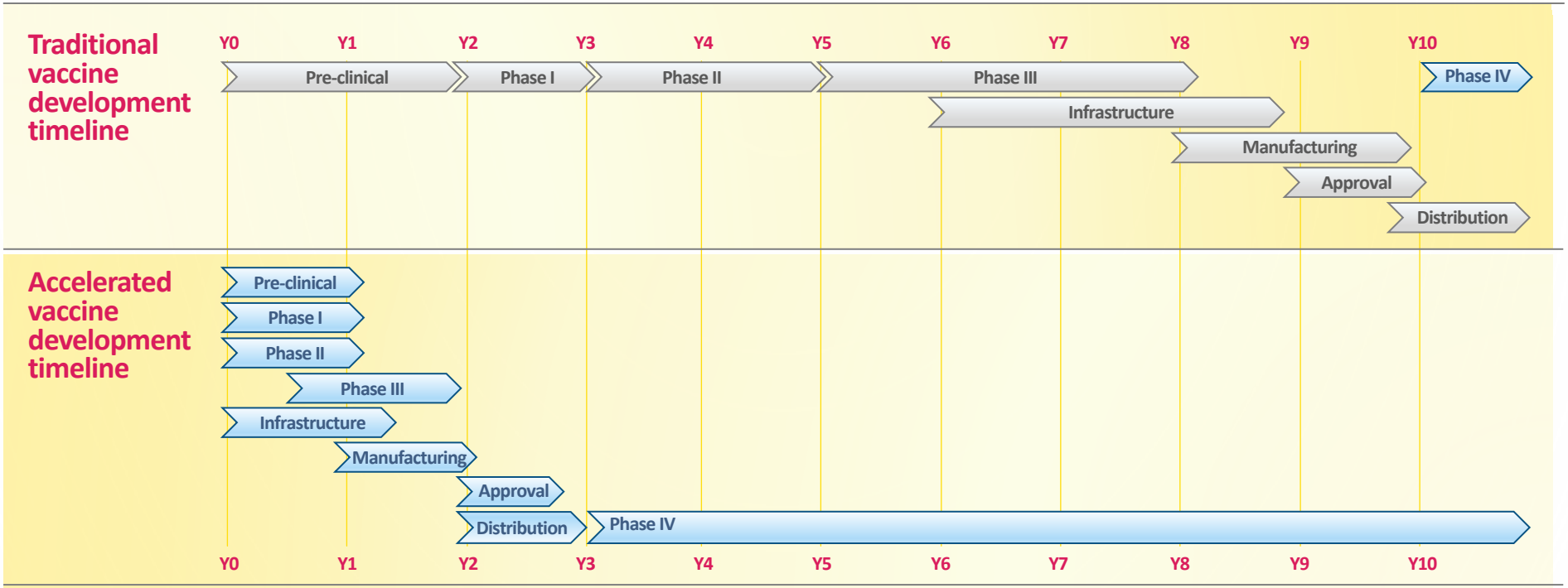
Phase III clinical trial

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

COVID-19 vaccine accelerated development



- Normal vaccine development performs each step in sequence
- To accelerate COVID-19 vaccine development, **steps are done in parallel**
- 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 02 October 2020 there are **42 COVID-19 candidate vaccines** in clinical evaluation of which **10 in Phase III trials**
- There are another **151 candidate vaccines in preclinical** evaluation
- Phase III trials usually require **30,000 or more participants**
- All top candidate vaccines are for **intra-muscular** injection
- Most are designed for a **two-dose** schedule (exceptions with a * in table are single dose)

10 CANIDATE VACCINES IN PHASE III CLINICAL EVALUATION	VACCINE PLATFORM	LOCATION OF PHASE III STUDIES
Sinovac	Inactivated virus	Brazil
Wuhan Institute of Biological Products / Sinopharm	Inactivated virus	United Arab Emirates
Beijing Institute of Biological Products / Sinopharm	Inactivated virus	China
University of Oxford / AstraZeneca	Viral vector *	United States of America
CanSino Biological Inc. / Beijing Institute of Biotechnology	Viral vector *	Pakistan
Gamaleya Research Institute	Viral vector	Russia
Janssen Pharmaceutical Companies	Viral vector	USA, Brazil, Colombia, Peru, Mexico, Philippines, South Africa
Novavax	Protein subunit	The United Kingdom
Moderna / NIAID	RNA	USA
BioNTech / Fosun Pharma / Pfizer	RNA	USA, Argentina, Brazil

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

* Single dose schedule

Immunogens used to develop viral vaccines

- Vaccines are being developed with different technologies — some well-known and others completely new for human vaccines, such as peptide and nucleic acid technologies

IMMUNOGEN	HOW IT WORKS	ADVANTAGE	DISADVANTAGE	EXAMPLE of vaccines
Attenuated live virus	Live virus but doesn't cause disease	Induces same response as natural infection	Not recommended for pregnant women and immunocompromised persons	Measles, rubella, mumps, yellow fever, smallpox (vaccinia)
Whole inactivated virus	Inactivated dead virus	Induces strong antibody response	Requires large quantities of virus	Influenza, rabies hepatitis A
Protein subunit	A protein derived from a pathogen	May have fewer side effects than whole virus (redness, swelling at injection site)	May be poorly immunogenic; complex process	Influenza
Recombinant	Host cell is used to express an antigen	No need to produce the whole virus	May be poorly immunogenic; High cost	Hepatitis B
Peptides	Synthetic produced fragment of an antigen	Rapid development	Poorly immunogenic; High cost	*COVID-19 vaccines in development*
Replicating or non-replicating viral vector	Viral pathogen expressed on a safe virus that doesn't cause disease	Rapid development	Prior exposure to vector virus (eg. adenovirus) may reduce immunogenicity	Ebola
Nucleic acid	DNA or RNA coding for a viral protein	Strong cellular immunity; rapid development	Relatively low antibody response	*COVID-19 vaccines in development*

Vaccine development

There is no direct correlation between the trial phase of vaccine and its superiority or future success.

A vaccine reaching phase 3 would not necessarily indicate that it is better than a vaccine in phase 1 or phase 2.

Why so many trials?

There are many different COVID-19 vaccines in development 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.

Why so many trials?

To increase the chances of success (given the high level of attrition during vaccine development), we must test all candidate vaccines until they fail. WHO is working to ensure that all of them have the chance of being tested at the initial stage of development

The challenges and efforts needed to rapidly develop, evaluate and produce this at scale are enormous. It is vital to evaluate as many vaccines as possible as it cannot be predicted how many will turn out to be viable.

At the same time, it is important to consider that not all vaccine manufacturers with products in clinical studies have the capacity to scale up their production and distribution to respond to global demand

How WHO help ensure ALL vaccines are evaluated?

Establishing robust and transparent processes
to assess preclinical evaluation and rigorously identify the few vaccines with the greatest promise to join Phase 3 trials

Convening international experts to design robust trial designs

Working with partners, clinical research networks and sites to find solutions to the needs and addressing the challenges for implementation

World Health Organization

R&DBlueprint
Powering research to prevent epidemics

What will be the presentation of the COVID-19 vaccines?
This information is still unknown; however, vaccines will likely come in multidose packaging.

How many doses will be needed?
This information is still unknown. If more than one dose is required, the number of weeks or months between doses is still being researched.

What could be the cold chain requirements of COVID-19 vaccines? (Meeting on 10/16)
While most of the COVID-19 candidate vaccines are expected to present similar cold chain requirements as existing vaccines (between 2-8°C), those developed using nucleic acids (DNA or RNA) might require lower temperatures such as -70°C or -80°C.

What could be the administration routes of COVID-19 vaccines?

Will it be possible to co-administer COVID-19 vaccines with other existing vaccines against other pathogens?

Will it be the same COVID-19 vaccine for pediatric and adult uses?
This information is still unknown. Future studies will assess it.

At this moment, there are no SARS-CoV-2 vaccines licensed by the World Health Organization (WHO) for the virus causing the COVID-19 pandemic

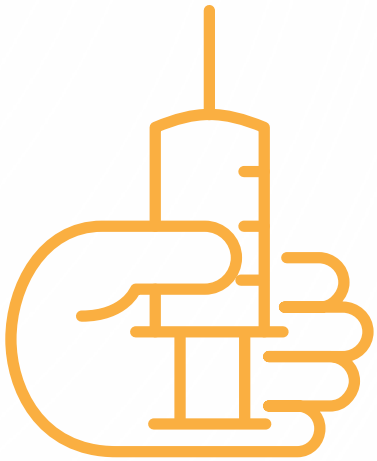
Thank You

Resources on COVID-19 vaccine development

- **WHO Target Product Profile for COVID-19 vaccine**
  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.
- **Vaccine landscape**
  Landscape documents prepared by the WHO for information purposes concerning the 2019-2020 global development of new COVID-19 vaccines.
- **Solidarity Vaccine Trial**
  This large, international, randomized controlled clinical trial is designed to enable an expeditious, agile and concurrent evaluation of the benefits and risks of multiple candidate preventive vaccines against COVID-19 at international sites with sufficient COVID-19 attack rates.
- **Access to COVID Tools (ACT) Accelerator**
  The vaccines pillar of the ACT Accelerator, convened is speeding up the search for an effective vaccine for all countries.
- **Covax facility (WHO) Covax explained (GAVI) COVAX (CEPI)**
- CEPI, Gavi and WHO launched COVAX to ensure equitable access to COVID-19 vaccines and end the acute phase of the pandemic by the end of 2021.
- **WHO Guidance on ethics of vaccine allocation**
  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.

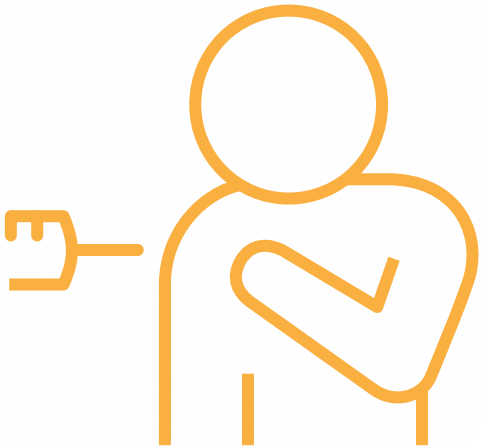
How vaccines work

- Vaccines greatly reduce the risk of infection by training the immune system to recognize and fight pathogens such as viruses or bacteria
- Vaccines safely deliver an **immunogen** which is a *specific type of antigen that elicits an immune response*, to train the immune system to recognize the pathogen when it is encountered naturally.



How vaccines are delivered

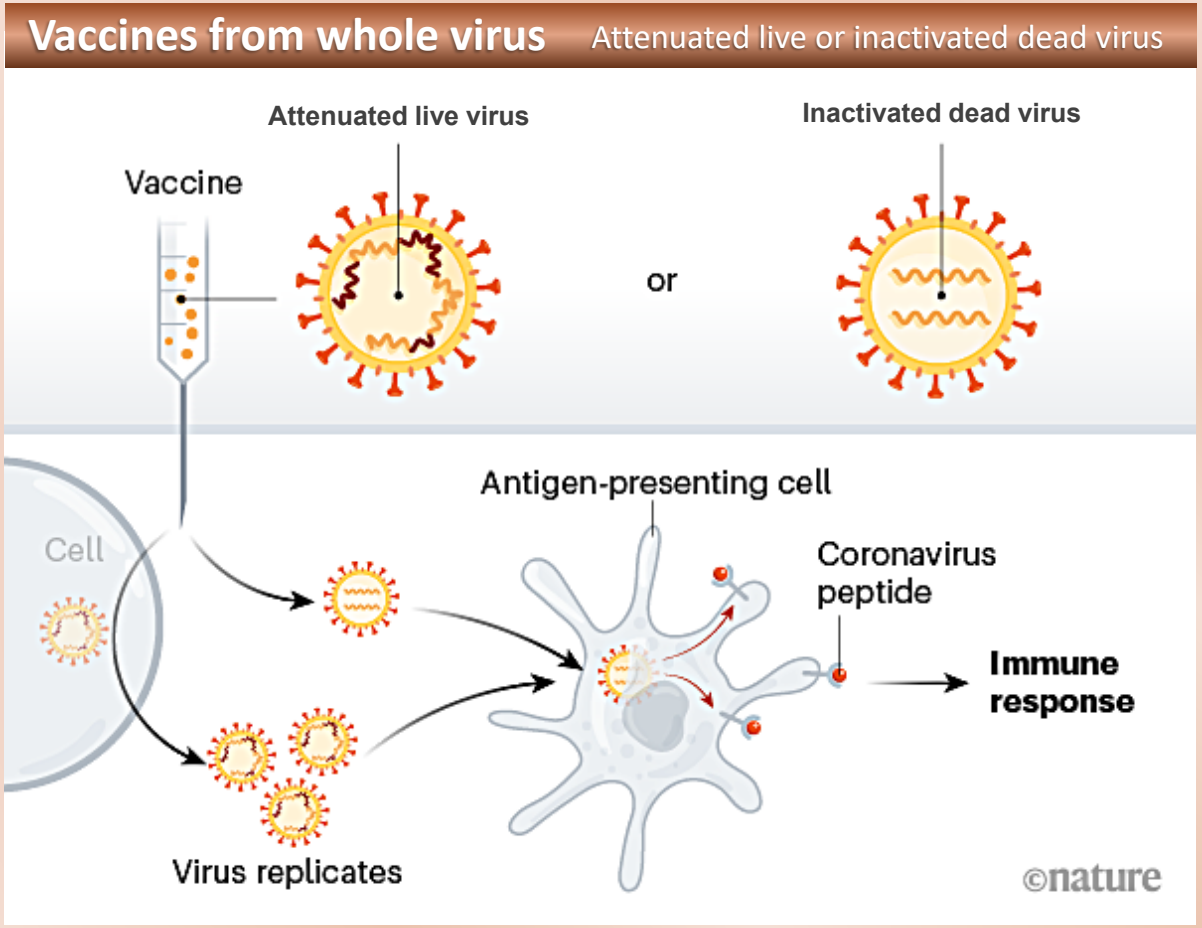
- A vaccine can be administered through different routes, for example injection in the muscle or under the skin or via the oral route.
- Vaccines sometimes require **more than one dose** to:
  - build complete immunity
  - give a ‘booster’ dose when immunity wears off
  - immunize people against viruses causing disease that may be different from season to season, for example, the yearly flu vaccine



Virus vaccines

- **Virus is selected, modified (weakened) or completely inactivated** so that it will not cause disease

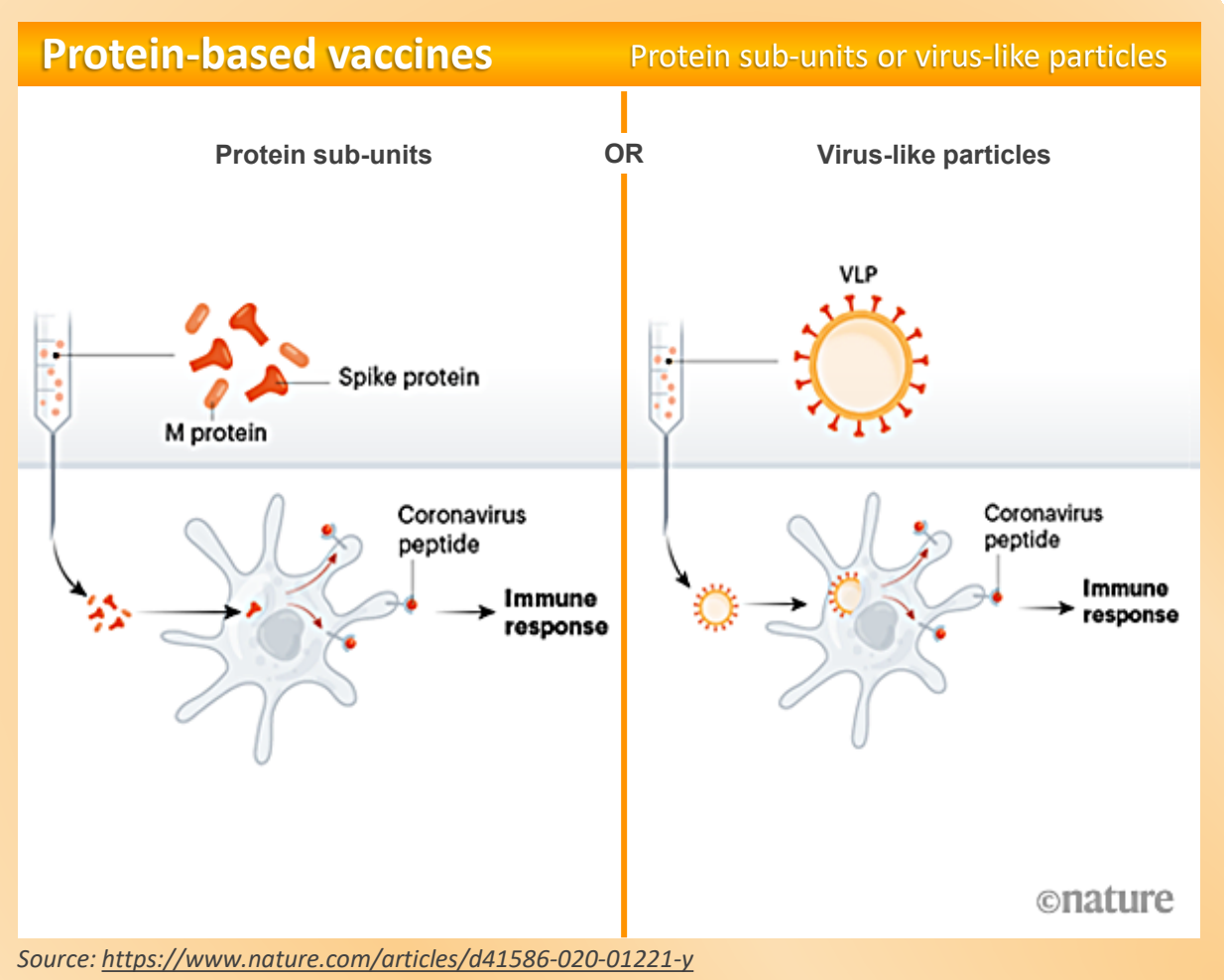
Note:
This illustration shows injectable vaccines. Some vaccines in this category are administered orally



Source: https://www.nature.com/articles/d41586-020-01221-y

Protein-based vaccines

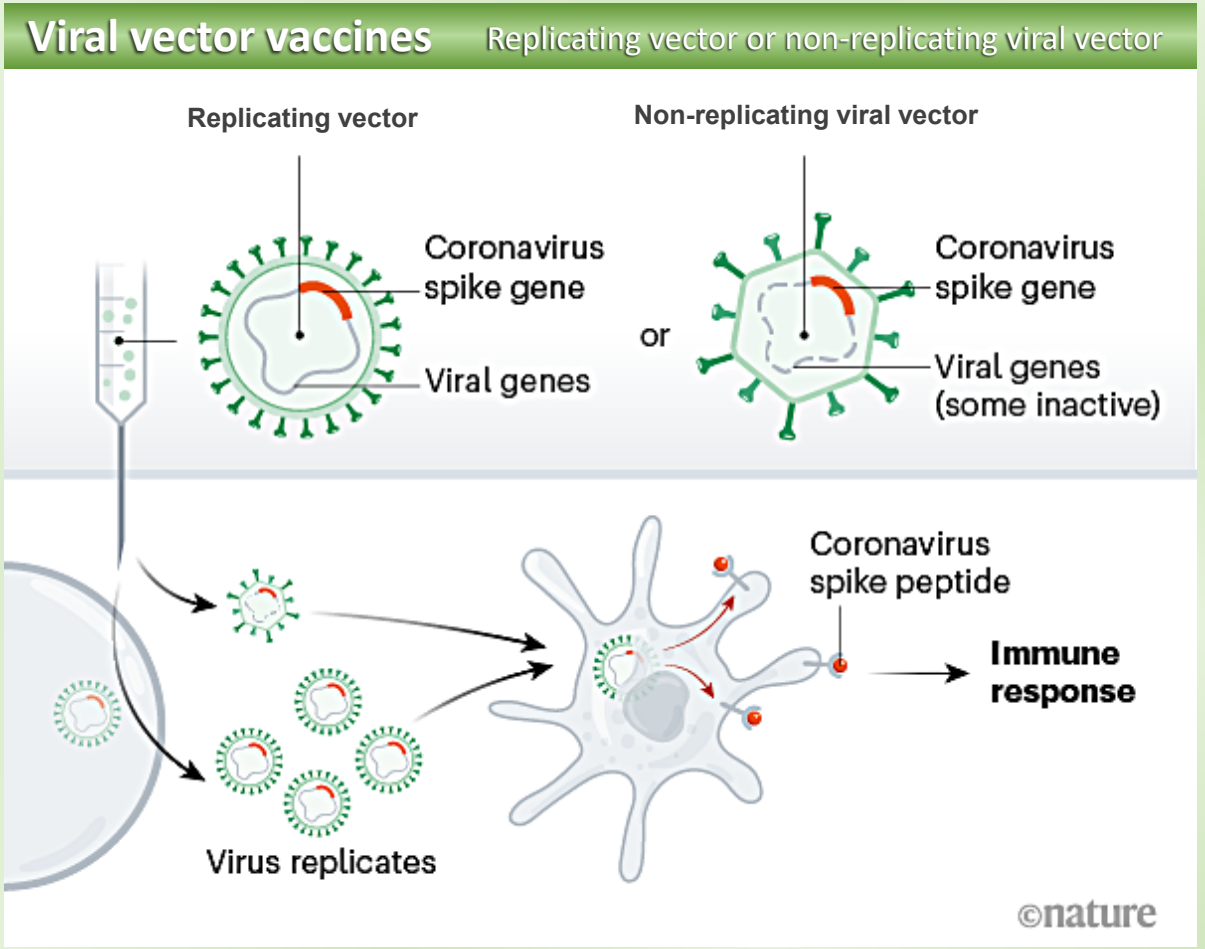
- **A protein is extracted from the virus** (alive or inactivated), purified, and injected as a vaccine
- For coronavirus, this is most commonly the spike protein
- Virus-like particles work in the same way



Source: https://www.nature.com/articles/d41586-020-01221-y

Viral vector vaccines

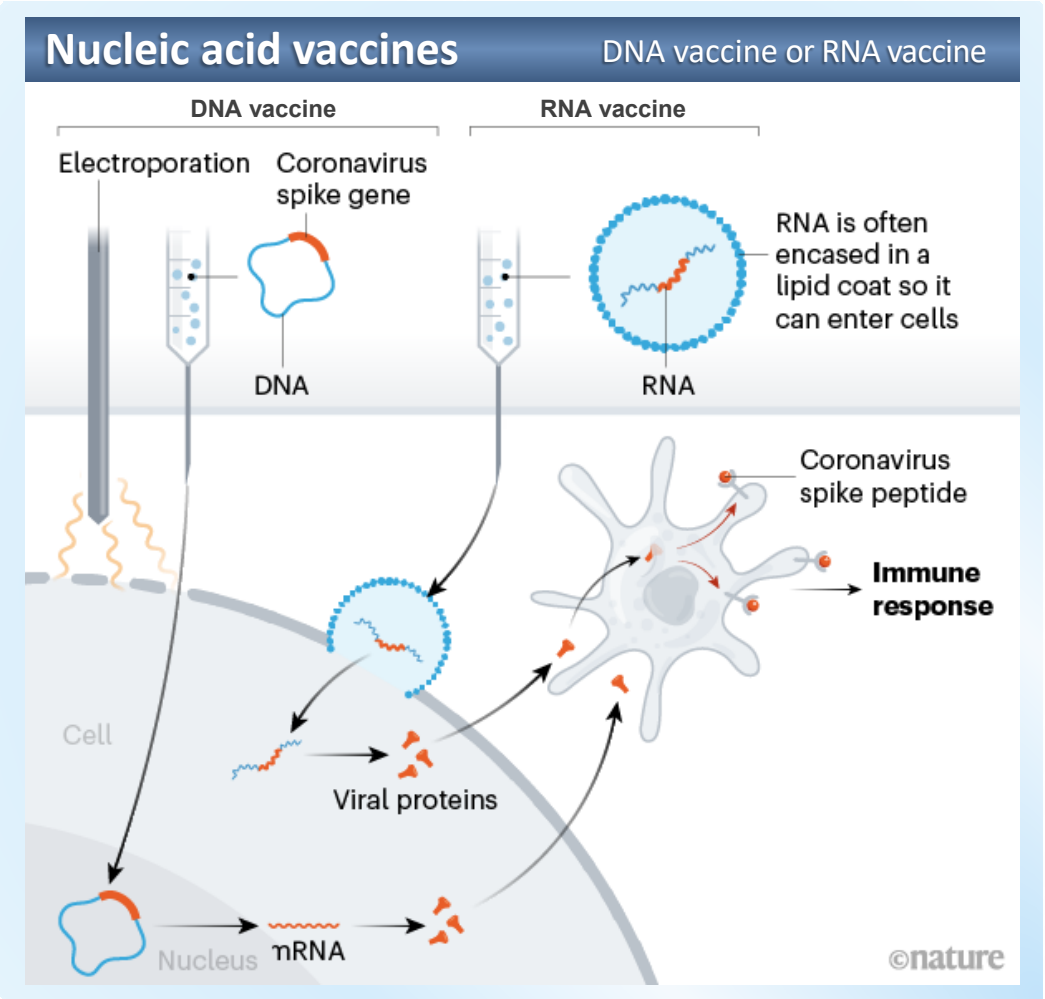
- **The gene for a pathogen protein is inserted into a different virus** that can infect someone without causing disease
- The safe virus serves as a 'platform' or 'vector' to deliver the protein that triggers an immune response
- The safe virus is then injected as a vaccine
- Some replicate (reproduce) in the body and some do not



Source: https://www.nature.com/articles/d41586-020-01221-y

Nucleic acid vaccines

- Instead of a virus, a protein antigen, or a virus expressing the protein, **nucleic acid coding for the antigen is injected**
- DNA plasmid: enters nucleus, translated to mRNA for expression of protein
- Or mRNA can be injected. More direct (no translation required) but less stable than DNA
- This is new technology – no other vaccines for human use have used this



Source: https://www.nature.com/articles/d41586-020-01221-y