COVID-19 Update

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Road to a COVID-19 Vaccine
Select vaccines by clinical trial start date

RNA and DNA vaccines

Other vaccine types

2020


- CanSino and the A.M.M.S.
- Moderna
- BioNTech and Pfizer
- Inovio Pharmaceuticals
- Sinovac
- Wuhan Institute and Sinopharm
- U. of Oxford
- Imperial College
- Novavax
- CureVac
- Sanofi and GSK
- Vaxart
- Alimmune
- Janssen

Uses 1 microgram of mRNA, meaning it could be more easily mass produced

Exploring a new form of oral vaccine, which has never been licensed
Vaccines in Development

<table>
<thead>
<tr>
<th>Virus</th>
<th>Viral vector</th>
<th>Nucleic acid</th>
<th>Protein-based</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactivated</td>
<td>Replicating</td>
<td>DNA</td>
<td>Protein subunit</td>
</tr>
<tr>
<td>Weakened</td>
<td>Non-replicating</td>
<td>RNA</td>
<td>Virus-like particles</td>
</tr>
</tbody>
</table>

- Virus: Inactivated, Weakened
- Viral vector: Replicating, Non-replicating
- Nucleic acid: DNA, RNA
- Protein-based: Protein subunit, Virus-like particles

Number of vaccines in development:

- Virus: 5
- Viral vector: 10
- Nucleic acid: 15
- Protein-based: 20
- Other*: 30

SARS-CoV-2:
- Spike (S) protein
- Cell membrane
- Transmembrane ACE-2
- Infection

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**Virus Vaccines**

**Weakened virus**
A virus is conventionally weakened for a vaccine by being passed through animal or human cells until it picks up mutations that make it less able to cause disease. Codagenix in Farmingdale, New York, is working with the Serum Institute of India, a vaccine manufacturer in Pune, to weaken SARS-CoV-2 by altering its genetic code so that viral proteins are produced less efficiently.

**Inactivated virus**
In these vaccines, the virus is rendered uninfectious using chemicals, such as formaldehyde, or heat. Making them, however, requires starting with large quantities of infectious virus.

**Viral-Vector Vaccines**

**Replicating viral vector (such as weakened measles)**
The newly approved Ebola vaccine is an example of a viral-vector vaccine that replicates within cells. Such vaccines tend to be safe and provoke a strong immune response. Existing immunity to the vector could blunt the vaccine’s effectiveness, however.

**Non-replicating viral vector (such as adenovirus)**
No licensed vaccines use this method, but they have a long history in gene therapy. Booster shots can be needed to induce long-lasting immunity. US-based drug giant Johnson & Johnson is working on this approach.

[Diagram showing the process of vaccine production and immunity induction for weakened and inactivated viruses, as well as viral-vector vaccines.]
NUCLEIC-ACID VACCINES

DNA vaccine
- Electrooporation
- Coronavirus spike gene

RNA vaccine
- RNA is often encased in a lipid coat so it can enter cells

A process called electroporation creates pores in membranes to increase uptake of DNA into a cell.

RNA- and DNA-based vaccines are safe and easy to develop: to produce them involves making genetic material only, not the virus. But they are unproven: no licensed vaccines use this technology.

PROTEIN-BASED VACCINES

Protein subunits
Twenty-eight teams are working on vaccines with viral protein subunits — most are focusing on the virus’s spike protein or a key part of it called the receptor binding domain. Similar vaccines against the SARS virus protected monkeys against infection but haven’t been tested in people. To work, these vaccines might require adjuvants — immune-stimulating molecules delivered alongside the vaccine — as well as multiple doses.

Virus-like particles
Empty virus shells mimic the coronavirus structure, but aren’t infectious because they lack genetic material. Five teams are working on 'virus-like particle' (VLP) vaccines, which can trigger a strong immune response, but can be difficult to manufacture.
Years and years, at minimum

The vaccine development process has typically taken a decade or longer.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Time (years or months)</th>
</tr>
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<tbody>
<tr>
<td>Varicella</td>
<td>28</td>
</tr>
<tr>
<td>FluMist</td>
<td>28</td>
</tr>
<tr>
<td>Human papillomavirus</td>
<td>15</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>15</td>
</tr>
<tr>
<td>Pediatric combination</td>
<td>11</td>
</tr>
<tr>
<td>Covid-19 goal</td>
<td>18 months</td>
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</tbody>
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Note: Rotavirus and HPV vaccines include time from filing of the first investigational new drug to approval. Source: “Plotkin’s Vaccines” (7th edition)