



ARIZONA DEPARTMENT OF HEALTH SERVICES

Arizona Vaccine News

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Health and Wellness for all Arizonans

Special COVID-19 and Influenza Vaccines Edition

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Many COVID-19 Vaccines Are Under Development

- There were 115 COVID-19 vaccines being worked on as of April 8, 2020. See *Nature*, [April 9, 2020](#).
- The World Health Organization has published a list of COVID-19 vaccines in clinical trials as of [August 13, 2020](#).
- There will need to be multiple effective vaccines in order to have enough supply to immunize the U.S. and the entire world.
- Vaccines platforms include RNA, DNA, protein subunit, replicating virus, non-replicating virus, vaccine-like particles, and inactivated virus vaccines.



Information on Volunteering for a COVID-19 Vaccine Clinical Study

- COVID-19 vaccine clinical study sites are opening in the Phoenix and Tucson areas.
- Information on volunteering can be found at www.coronaviruspreventionnetwork.org.

FDA Commitment to Unwavering Regulatory Safeguards for COVID-19 Vaccines

- Vaccine development comes with significant financial risk to the vaccine manufacturer.
- To facilitate the rapid development of COVID-19 vaccines, the US government launched Operation Warp Speed (OWS) in May 2020 in order to compress the time for vaccine development.
 - Part of OWS involves up-front financial commitments to vaccine manufacturers. This allows them to make millions of doses of candidate vaccines while clinical trials are still ongoing.
 - The result will be that once a vaccine's clinical trial shows that the vaccine is effective and safe, many millions of doses will quickly be ready for distribution as soon as it is approved by the Food and Drug Administration (FDA).
- The FDA has unequivocally stated that candidate COVID-19 vaccines will be reviewed according to the established legal and regulatory standards for medical products to ensure scientific integrity and vaccine safety.

For further details, see JAMA, [August 7, 2020](#).

Highlights on COVID-19 Vaccines from ACIP Meetings, June 24, 2020 and July 29, 2020

- Slides are available from the meetings of the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention from [June 24](#) and [July 29](#).
- The following information is a summary of these two ACIP meetings, written by Karen Lewis M.D., for the benefit of those who would like to read more details about ACIP discussions regarding COVID-19 vaccines.

Operation Warp Speed

- OWS leverages U.S. government and private resources to accelerate development of COVID-19 vaccines. Compressing time lines for COVID-19 vaccine development involves increasing funding and optimizing resources but will not involve compressing clinical testing requirements.
- There will be semi-independent harmonized clinical trials (a common definition of COVID-19 disease, common testing endpoints, common immune assays [both antibody and cellular]; common measure of efficacy, a common Data and Safety Monitoring Board, etc.).
- The FDA will continue to have independent overview of safety and efficacy of COVID-19 vaccine development. Manufacturers will be following the FDA [Guidance](#) for Industry on COVID-19 Vaccine Development.



Traditional FDA Vaccine Licensure versus an Emergency Use Authorization (EUA)

- FDA licensing requires demonstration of vaccine safety, effectiveness and consistent manufacturing to ensure continued safety and effectiveness of the licensed vaccine.
- The traditional FDA approval pathway takes many months.
- Licensing of vaccines under an [EUA](#) can occur when there is a declaration by the Health and Human Services Secretary of an emergency situation leading to serious or life-threatening disease or condition, when there is evidence of effectiveness for the product intended to address the emergency, when the known and potential benefits of the product outweigh the known and potential risks of the product, and when there is no adequate, approved, and available alternative.

COVID-19 Vaccine Safety

- Antibodies that bind to viruses without neutralizing the viruses can cause severe disease through increased viral replication or formation of immune complexes that deposit in tissue and activate complement pathways associated with inflammation.
- Previous candidate vaccines have resulted in enhanced disease:
 - Respiratory syncytial virus (RSV). In the 1960s, an experimental RSV vaccine was developed using formalin-inactivated virus. Recipients of this vaccine had more severe disease when infected with RSV. Two of the immunized infants died.
 - Further evaluation showed that the formalin had changed the structure of the RSV protein so that it did not stimulate neutralizing antibodies. Also, the T-cell responses were Th-2 biased (allergic), resulting in vaccine associated enhanced respiratory disease (VAERD).
 - Autopsies on the two infants found eosinophils in their lung tissue.
 - Dengue. Immunized children 2-4 years old who had previously been infected with one of the four serotypes of dengue were protected by the dengue vaccine. However, seronegative children 2-4 years old did not develop protective neutralizing antibodies. When these children were later infected with dengue, the vaccine-induced antibodies resulted in antibody enhancement of viral entry into cells and more severe disease (antibody-enhanced disease [AED]).
- Preventing similar problems with COVID-19 vaccines will involve making sure that the antigen is correct, that the vaccines produce high quality neutralizing antibodies, and that the cellular responses are Th-1 biased cellular responses (instead of Th-2 biased).

COVID-19 Vaccines Trials

- SARS-CoV-2 virus has external spike protein whose receptor binding domain allows viral entry into human cells. **Vaccine development focuses on producing immunity to this spike protein.**
- For each candidate vaccine, phase 3 clinical trials will involve about 30,000 people (ages 18 years and older) with a 1:1 ratio of vaccine to placebo. Efficacy will be measured by how well the vaccine protects against COVID-19 compared to placebo recipients.
- COVID-19 vaccines may require 2 doses separated by 21-28 days for optimal immunity.



Specific COVID-19 Vaccines Being Studied in Humans

- Oxford University/AstraZeneca. A non-replicating chimpanzee adenovirus that expresses the SARS-CoV-2 spike protein.
- Moderna/National Institute of Allergy and Infectious Diseases. Lipid nanoparticles containing mRNA that codes for the SARS-CoV-2 spike protein.
- Pfizer/BioNTech. Several lipid nanoparticle mRNA vaccines are being tested.
- Janssen (Johnson and Johnson): A non-replicating human adenovirus 26 that expresses the SARS-CoV-2 spike protein.
- Novavax. A SARS-CoV-2 spike protein subunit vaccine using a recombinant glycoprotein nanoparticle combined with a matrix M adjuvant.
- Inovio. A DNA plasmid vaccine that codes for the spike protein and is administered by electroporation. Electroporation is a microbiology technique in which an electrical pulse is applied to cells in order to transiently increase the permeability of cell membranes, allowing the DNA vaccine to be introduced into the cells' nuclei.

COVID-19 Vaccine Prioritization Considerations

- Goals for the COVID-19 vaccine program
 - Safety and effectiveness
 - Reduce SARS-CoV-2 transmission, morbidity, and mortality
 - Maintain healthcare capacity
 - Minimize disruption to society and economy
 - Promote equity in allocation and distribution
- Multiple populations are at higher risk for COVID-19 disease and severity
 - Occupations with higher risk are healthcare providers and agriculture workers (e.g. there have been COVID-19 outbreaks in meat-packing plants).
 - Individuals at risk of severe COVID-19 disease include people in long-term care facilities, older adults (65+), those with underlying medical conditions, those with social risk factors (American Indian, Black or Hispanic race/ethnic groups), those in correctional facilities and those experiencing homelessness.
- When initial vaccine supply is constrained, the focus will be on target populations where high coverage is essential for public health (e.g., healthcare and essential workers; individuals in long-term care and assisted living facility residents).
- As there is greater vaccine supply, there will be vaccine targeting of older adults, persons with underlying health conditions, and racial/ethnic minorities.
- Vaccine will be available for the general population once there is adequate vaccine supply.



Challenges for COVID-19 Vaccine Implementation

- Many vaccines will require a 2-dose series, others just one dose.
- There will likely be multiple vaccine products that are not interchangeable. People who receive vaccine that requires 2 doses need to receive the second dose from the same product.
- There are likely to be varying cold-chain requirements.
- Vaccine administration will need to be done in a socially-distanced way.
- Vaccine efficacy and adverse event profiles may differ in different populations.
- Vaccine clinical trials still need to be done for children and pregnant women.

CDC Influenza Vaccine Guidance for the 2020-2021 Season

- Quadrivalent vaccines specifically for ≥ 65 -year-old patients are now available (Fluzone High-Dose Quadrivalent and Fluvad Quadrivalent).
 - The dose of Fluzone High-Dose Quadrivalent has been increased to 0.7 mL.
- Additional contraindications to live-attenuated influenza vaccine have been added:
 - Anatomic or functional asplenia
 - Cerebrospinal leak
 - Cochlear implant
 - Receipt of influenza antiviral medication within the previous 48 hours for oseltamivir and zanamivir, the previous 5 days for peramivir, and the previous 17 days for baloxavir
- Modification in the language of how to use influenza vaccine in people with a history of severe allergic reaction to eggs.

For more details, see *Morbidity and Mortality Weekly Report*, RR-8, [August 21, 2020](#).

- Note: During this COVID-19 pandemic, influenza vaccine will play an important role.
 - Decrease the risk of acquiring influenza, a febrile illness with fever and cough, that could raise concerns of possible COVID-19 infection.
 - Decrease influenza-related hospitalizations and ICU care, thereby resulting in more hospital beds available for COVID-19 patients.

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