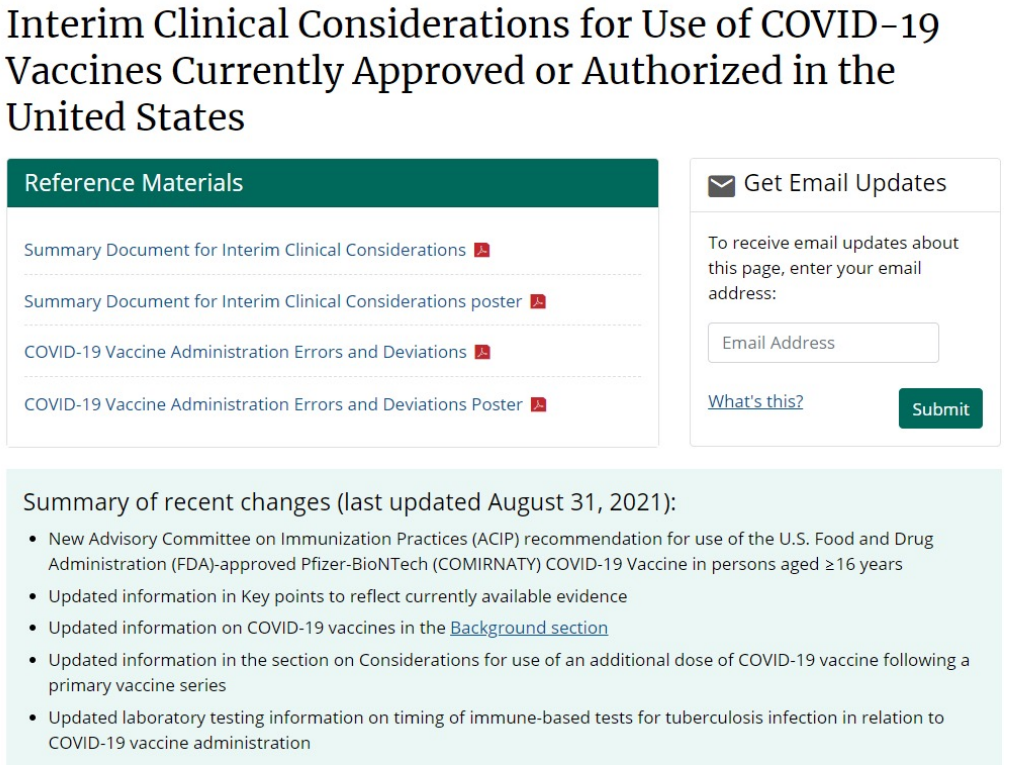
COVID-19 Vaccination Clinical Considerations

September 16, 2021

Key points: Interim clinical considerations for COVID-19 vaccines

- **COVID-19 vaccination is recommended for all people 12 years and older.**
- Recommendations apply to the use of
  - Food and Drug Administration (FDA)-approved Pfizer-BioNTech (COMIRNATY) COVID-19 Vaccine in persons aged ≥16 years.
  - Pfizer-BioNTech, Moderna, and Janssen (Johnson & Johnson) COVID-19 vaccines under the FDA's Emergency Use Authorization (EUA).
- Guidance may change as further information becomes available.


Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Approved or Authorized in the United States

Reference Materials

Summary Document for Interim Clinical Considerations

Summary Document for Interim Clinical Considerations poster

COVID-19 Vaccine Administration Errors and Deviations

COVID-19 Vaccine Administration Errors and Deviations Poster

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Summary of recent changes (last updated August 31, 2021):

- New Advisory Committee on Immunization Practices (ACIP) recommendation for use of the U.S. Food and Drug Administration (FDA)-approved Pfizer-BioNTech (COMIRNATY) COVID-19 Vaccine in persons aged ≥16 years
- Updated information in Key points to reflect currently available evidence
- Updated information on COVID-19 vaccines in the Background section
- Updated information in the section on Considerations for use of an additional dose of COVID-19 vaccine following a primary vaccine series
- Updated laboratory testing information on timing of immune-based tests for tuberculosis infection in relation to COVID-19 vaccine administration

https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

Key messages

- COVID-19 vaccination is recommended for everyone 12 years and older in the United States.
- COVID-19 vaccines currently approved or authorized by FDA **are highly effective** in preventing serious outcomes, including hospitalization and death.
- **Available evidence indicates these vaccines offer protection against known variants, including the Delta variant (B.1.617.2), particularly against hospitalization and death.**
- Maximizing the proportion of people in the United States who are fully vaccinated against COVID-19 remains critical to ending the COVID-19 pandemic.

Regulatory terminology for COVID-19 vaccines

- **Emergency Use Authorization (EUA)**
  A mechanism to facilitate the availability and use of medical products, including vaccines, during public health emergencies such as the current COVID-19 pandemic.
  - Under an EUA, the FDA can make a product available to the public based on the best available evidence, without waiting for all the evidence required for FDA approval.
  - Following the issuance of an EUA, the manufacturer continues safety and effectiveness trials.

- **FDA Approved**
  FDA-approved vaccines have undergone the agency's standard review process for quality, safety, and effectiveness. FDA conducts its own analyses to ensure that vaccines meet the agency's standards for approval.

COVID-19 vaccines approved or authorized by the FDA for prevention of COVID-19

- FDA **approved** the licensure of COMIRNATY (COVID-19 Vaccine, mRNA) made by Pfizer for BioNTech as a 2-dose series in persons aged ≥16 years (August 23, 2021).
  - The FDA-approved Pfizer-BioNTech product COMIRNATY and the FDA-authorized Pfizer-BioNTech COVID-19 Vaccine are identical and can be used interchangeably.
- FDA has **authorized** three vaccines under EUA:
  - Pfizer-BioNTech COVID-19 Vaccine (aged 12-15 years)
  - Moderna COVID-19 Vaccine ≥18 years
  - Janssen COVID-19 Vaccine ≥18 years
- FDA has **authorized** an additional (3rd dose) of mRNA vaccines for persons with certain immunocompromising conditions:
  - Pfizer-BioNTech COVID-19 (COMIRNATY) Vaccine
  - Moderna COVID-19 Vaccine ≥18 years

Dosing and administration

	Pfizer-BioNTech	Moderna	Janssen
FDA-approved age groups	≥ 16 years		
FDA-authorized age groups	≥ 12-15 years	≥ 18 years	≥ 18 years
Number of doses in series	2 doses	2 doses	1 dose
Interval between 1st and 2nd doses*	21 days (3 weeks)	28 days (1 month)	NA
Dose volume	0.3 ml	0.5 ml	0.5 ml
Route	Intramuscular	Intramuscular	Intramuscular

*The second dose of Pfizer-BioNTech and Moderna vaccines should be administered as close to the recommended interval as possible, but not earlier than recommended (i.e., 3 weeks [Pfizer-BioNTech] or 1 month [Moderna]). However, individuals who receive the second dose up to 4 days before or at any time after the recommended date can be considered fully vaccinated.

Fully vaccinated people

People are considered fully vaccinated against COVID-19:

- 2 weeks after receiving the second dose in a 2-dose series (Pfizer-BioNTech, Moderna).
- 2 weeks after receiving a single dose in a 1-dose series (Janssen).

People who have a contraindication to vaccination or do not complete a vaccination series for any reason are **not** considered **fully vaccinated**.

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html#_ednref1

Improve 2nd dose compliance for mRNA COVID-19 vaccines

- Provide the required COVID-19 vaccination record cards to vaccine recipients. Ask them to bring their card to the second-dose appointment. Encourage them to make a backup copy of the card, either a physical copy or a smartphone photo.

- Encourage vaccine recipients to enroll in *v-safe*, a free smartphone-based tool that uses text messaging for personalized health check-ins as well as second-dose reminders and *VaxText*SM, a free text message-based platform for COVID-19 vaccination second-dose reminders.

- Record each recipient's vaccination in the immunization information system (IIS).

- Record vaccine administration information in the patient's medical record.

- Make an appointment for the second dose during the first dose.

https://www.cdc.gov/vaccines/covid-19/reporting/vaxtext/index.html

Interchangeability of COVID-19 vaccines

- Because data on the safety and efficacy of a mixed-product series remain limited, COVID-19 vaccines are **not interchangeable** with each other.
- Better to delay the 2nd dose of an mRNA vaccine (Pfizer-BioNTech, Moderna) and receive the same product than to receive a mixed series of different products.
- Exceptional situations include:
  - the mRNA vaccine used for first dose cannot be determined or is no longer available, any mRNA COVID-19 vaccine can be used for 2nd dose
  - a person received the 1st dose of an mRNA vaccine but is unable to complete the series with either the same or a different mRNA vaccine (e.g., due to a contraindication), a single dose of Janssen Vaccine may be considered at a minimum interval of 28 days from the mRNA vaccine dose.

People vaccinated outside the United States

- People vaccinated outside the United States with an FDA-approved or -authorized COVID-19 vaccine or with a World Health Organization (WHO) emergency use listed COVID-19 vaccine that have received all recommended doses are considered fully vaccinated and **do not need** any additional doses.
- People who received the first dose of a two-dose series of an FDA-approved or -authorized COVID-19 vaccine outside the United States **do not need to restart** the series but should receive the second dose as close to the recommended interval as possible.
- People who received all or some of the recommended doses of COVID-19 vaccine NOT approved by or authorized by FDA or listed for emergency use by WHO, **may be offered** a complete FDA-approved or –authorized COVID-19 vaccine series.
- People who have not received all recommended doses of a COVID-19 vaccine listed for emergency use by WHO **may be offered** a complete FDA-approved or -authorized COVID-19 vaccine series.[1,2]

[1]Limited data are available on the safety or efficacy of receiving a COVID-19 vaccine currently authorized in the United States after receipt of a non-FDA-authorized COVID-19 vaccine.
[2]Minimum interval between the last dose of a non-FDA authorized vaccine or a WHO-listed vaccine and an FDA-authorized COVID-19 vaccine is 28 days.

People vaccinated outside the United States (continued)

COVID-19 vaccines listed for emergency use by WHO as of August 31, 2021:

- Pfizer-BioNTech COVID-19 vaccines (COMIRNATY, Tozinameran)
- AstraZeneca-Oxford COVID-19 vaccines (Covishield, Vaxzevria)
- Janssen (Johnson & Johnson) COVID-19 Vaccine
- Moderna COVID-19 Vaccine
- Sinopharm BIBP COVID-19 Vaccine
- Sinovac-CoronaVac COVID-19 Vaccine

People vaccinated as part of a clinical trial in the United States

For people in the United States who completed a COVID-19 vaccination series as part of a clinical trial involving a vaccine candidate not approved or authorized by FDA:

- If the clinical trial participant received the full series of a COVID-19 vaccine that is not approved or authorized by FDA but is listed for emergency use by WHO, **no additional doses** of an FDA-approved or -authorized COVID-19 vaccine are needed.
- When the participant is confirmed to have received “active” vaccine (not placebo), that participant can be considered fully vaccinated 2 weeks after completing the vaccine series.

Currently, **AstraZeneca COVID-19 Vaccine** meets these criteria.

People vaccinated as part of a clinical trial (continued)

For people in the United States who completed a COVID-19 vaccination series as part of a clinical trial involving a COVID-19 vaccine candidate that is not approved or authorized by FDA, **nor listed for emergency use by WHO:**

- When a participant is confirmed to have received "active" vaccine (not placebo) and vaccine efficacy has been independently confirmed (e.g., by a data and safety monitoring board), that participant can be considered fully vaccinated 2 weeks after completing the vaccine series.*

Currently, **Novavax COVID-19 Vaccine** meets these criteria.

- Novavax clinical trial participants who did not receive the full 2-dose series should follow current COVID-19 prevention measures and should be offered an FDA-approved or -authorized vaccine series.

***This does not imply that the vaccine has been approved or authorized by FDA or is recommended by CDC or ACIP.**

Considerations for coadministration

- Is the patient behind or at risk of becoming behind on recommended vaccines?
- What is their risk of vaccine-preventable disease (e.g., during an outbreak or occupational exposure)?
- What is the reactogenicity provide of the vaccines?

*Best practices for multiple injections can be found at: https://www.cdc.gov/vaccines/hcp/admin/administer-vaccines.html

Coadministration with other vaccines

COVID-19 vaccines and other vaccines **may be coadministered.***

- Coadministration considerations
- Administer the COVID-19 vaccine and vaccines that may be more likely to cause a local reaction in different limbs, if possible.
  - Consider reactogenicity profile of the vaccines.
  - Assess if patient is behind or at risk of becoming behind on recommended vaccines.
  - Evaluate patient's risk of vaccine-preventable disease (e.g., during an outbreak or occupational exposure).
- Extensive experience with non-COVID-19 vaccines indicates immunogenicity and adverse event profiles are generally similar when vaccines are administered simultaneously as when they are administered alone.
  - It is unknown whether the reactogenicity of COVID-19 vaccines increases with coadministration, including with vaccines known to be more reactogenic, such as adjuvant or live vaccines.

*Best practices for multiple injections can be found at: https://www.cdc.gov/vaccines/hcp/admin/administer-vaccines.html

People with a history of SARS-CoV-2 infection

- People should be offered vaccination regardless of their history of symptomatic or asymptomatic SARS-CoV-2 infection, including people with prolonged post-COVID-19 symptoms.
- Persons exhibiting symptomatic infection should not be vaccinated until they have recovered from acute illness *and* met all criteria for discontinuing isolation.
- Viral or serologic testing for acute or prior infection is not recommended for the purpose of deciding whether to vaccinate.

https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-in-home-patients.html
https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html

People with a history of multisystem inflammatory syndrome in children (MIS-C) or adults (MIS-A)

- No safety or efficacy data for COVID-19 vaccines for people with prior MIS-C or MIS-A.
- Consider delaying vaccination until recovery from illness *and* for 90 days after the date of diagnosis of MIS-C or MIS-A.*
- A conversation between the patient, their guardian(s), and a healthcare provider, may assist with decisions about the use of a COVID-19 vaccine.
- Consider referral to a specialist in infectious diseases, rheumatology, or cardiology for persons who develop MIS-C or MIS-A associated with a confirmed SARS-CoV-2 infection that occurs *after* receipt of a COVID-19 vaccine. Healthcare providers and health departments may also request a consultation from the Clinical Immunization Safety Assessment COVIDvax.

*Mechanisms of MIS-C and MIS-A are not well understood but include a dysregulated immune response to SARS-CoV-2 infection; it is unclear if the same dysregulated immune response would recur following reinfection with SARS-CoV-2 or in response to vaccination.

People who previously received passive antibody therapy for COVID-19

- No data are available on safety or efficacy of COVID-19 vaccination in people who received monoclonal antibodies* or convalescent plasma as part of COVID-19 treatment or post-exposure prophylaxis.
- To avoid interference with vaccine-induced immune responses, vaccination should be deferred at least 90 days for persons who receive passive antibody therapy before any COVID-19 vaccine dose.
- Receipt of passive antibody therapy in the past 90 days is not a contraindication to receipt of COVID-19 vaccine.

*Three anti-SARS-CoV-2 monoclonal antibody products currently have FDA Emergency Use Authorizations (EUAs): bamlanivimab plus etesevimab, casirivimab plus imdevimab, and sotrovimab.

Vaccinated people who subsequently develop COVID-19

- Prior receipt of a COVID-19 vaccine should not affect treatment decisions (including use of monoclonal antibodies, convalescent plasma, antiviral treatment, or corticosteroid administration) or timing of such treatments.
- For purposes of surveillance, infections in vaccinated people (i.e., breakthrough infections) are defined as detection of SARS-CoV-2 RNA or antigen in a detected on a respiratory specimen collected ≥14 days after completion of all recommended doses of an FDA-approved or FDA-authorized COVID-19 vaccine.
- COVID-19 infections in vaccinated people resulting in hospitalization or death should be reported to the Vaccine Adverse Event Reporting System (VAERS).

https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html

People with a known SARS-CoV-2 exposure or during COVID-19 outbreaks

- Unvaccinated people in the community or in outpatient settings with a known COVID-19 exposure should defer vaccination until their quarantine period has ended.
- COVID-19 vaccines are not recommended for outbreak management or postexposure prophylaxis; post-exposure prophylaxis with monoclonal antibodies is discussed elsewhere.
- Residents with known exposure or undergoing screening in congregate healthcare settings or non-healthcare settings may be vaccinated if they do not have any symptoms consistent with COVID-19, as exposure to and transmission of SARS-CoV-2 can occur repeatedly for long periods of time.

https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html
https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html

People with underlying medical conditions

- Any currently authorized or approved COVID-19 vaccine can be administered to people with underlying medical conditions but no contraindications to vaccination.
  - Clinical trials demonstrated similar safety and efficacy profiles in people with certain underlying medical conditions, including those that place them at increased risk for severe COVID-19, compared to persons without comorbidities.

- Healthcare personnel or health departments with complex COVID-19 vaccine safety questions not readily addressed by CDC guidance can request a consultation from the Clinical Immunization Safety Assessment COVIDvax.

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html
https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/index.html

Additional and booster doses of COVID-19 vaccines

There are two distinct potential uses for an extra vaccine dose:

- **Additional dose after an initial primary vaccine series**
  An additional vaccine dose might be administered when the initial immune response following a primary vaccine series is likely to be insufficient.

- **Booster dose**
  A vaccine dose administered when the initial sufficient immune response to a primary vaccine series is likely to have waned over time.

Considerations for use of an additional mRNA COVID-19 vaccine dose after an initial 2-dose vaccine series for immunocompromised people

- People with immunocompromising conditions or who take immunosuppressive medications or therapies are at increased risk for severe COVID-19 illness.

- For people with moderate to severe immune compromise due to a medical condition or immunosuppressive treatment, the potential to increase immune response coupled with an acceptable safety profile supports the use of an additional mRNA COVID-19 vaccine dose.

Qualifying immunocompromising conditions*

- Active treatment for solid tumor and hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of CAR-T-cell or hematopoietic stem cell transplant within 2 years of transplantation or taking immunosuppression therapy
- Moderate or severe primary immunodeficiency (e.g., DiGeorge, Wiskott-Aldrich syndromes)
- Advanced or untreated HIV infection: CD4 cell count <200/mm^3, history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV
- Active treatment with high-dose corticosteroids (≥20mg prednisone or equivalent per day for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, TNF blockers, and other immunosuppressive or immunomodulatory biologic agents

*ACIP General Best Practice Guidelines for Immunization; CDC Yellow Book; 2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host

Clinical considerations: additional dose of COVID-19 vaccine in immunocompromised people

- Patient's clinical team is best situated to determine the degree of immune compromise and appropriate timing of vaccination.
- Timing of COVID-19 vaccination should take into consideration current or planned immunosuppressive therapies and optimization of both the patient's medical condition and response to vaccine.
  - Whenever possible, additional dose (as well as primary vaccine series) should be given at least two weeks before initiation or resumption of immunosuppressive therapies.
- Factors to consider in assessing the general level of immune competence include disease severity, duration, clinical stability, complications, comorbidities, and any potentially immune-suppressing treatment.
- Utility of serologic testing or cellular immune testing to assess immune response to vaccination and guide clinical care (e.g., need for an additional dose) has not been established and is not recommended at this time.

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#considerations-additional-vaccine-dose

Implementation considerations: additional mRNA COVID-19 vaccine dose in immunocompromised people

- The additional dose should be the same mRNA vaccine product as the initial 2-dose mRNA COVID-19 primary vaccine series.
- Alternate mRNA product can be used if primary series product is not available.
- Until more data are available, the additional dose should be administered at least 28 days after completion of the initial primary series.
- Current data are insufficient to support the use of an additional mRNA COVID-19 vaccine dose after a single-dose Janssen COVID-19 vaccination in immunocompromised people.
- These clinical considerations for use of an additional dose of an mRNA COVID-19 vaccine apply *only* to people who are moderately or severely immunocompromised.

Important infection prevention measures for immunocompromised people

- All immunocompromised people, including those who receive an additional mRNA COVID-19 vaccine dose, should be counseled about their potentially reduced immune response to COVID-19 vaccination and continuing need to follow current prevention measures:*
  - Wear a mask.
  - Stay 6 feet away from people they don't live with.
  - Avoid crowds and poorly ventilated indoor spaces until advised otherwise by their healthcare provider.
- Close contacts of immunocompromised people should be strongly encouraged to be vaccinated against COVID-19.

* https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html

Myocarditis and pericarditis after vaccination with mRNA COVID-19 vaccines

Myocarditis (inflammation of the heart muscle) or pericarditis (inflammation of the lining around the heart) have occurred in some people after receipt of mRNA COVID-19 vaccines (Pfizer-BioNTech and Moderna).

- Cases have occurred predominantly in males aged 12-29 years.
- Symptoms typically developed within a few days after receipt of the 2nd dose.
- For patients who have been hospitalized, most were for short periods, with most achieving resolution of acute symptoms.
- Follow up is ongoing to identify and understand potential long-term outcomes among cases.

- Mechanisms that cause myocarditis or pericarditis after receipt of an mRNA COVID-19 vaccine are not well understood.
- Clinicians should:
  - Consult current clinical guidance for information on the evaluation and management of myocarditis or pericarditis.
  - Report all cases of myocarditis or pericarditis after COVID-19 vaccination to VAERS .

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html
https://vaers.hhs.gov/reportevent.html

Benefit-risk assessments for myocarditis and pericarditis after vaccination with mRNA COVID-19 vaccines

The Advisory Committee on Immunization Practices (ACIP) determined the benefits of using mRNA COVID-19 vaccines clearly outweigh the risks, including the risk of myocarditis or pericarditis.

- People receiving mRNA COVID-19 vaccines, esp. males aged 12-29 years, should be:
  - Made aware of the possibility they could develop myocarditis or pericarditis following receipt of mRNA COVID-19 vaccines or infection with SARS-CoV-2.
  - Counseled to seek care if symptoms of myocarditis or pericarditis develop after vaccination.
- Continued monitoring of patients' clinical course and long-term outcomes is important:
  - CDC is continuing to investigate cases after mRNA COVID-19 vaccination.
  - Post-vaccination cases of myocarditis or pericarditis should be reported to VAERS.

https://www.cdc.gov/mmwr/volumes/70/wr/mm7027e2.htm; https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html
https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine
Moderna COVID-19 Vaccine | FDA

Considerations for use of mRNA COVID-19 vaccines in people with a history of myocarditis or pericarditis (1)

*For people who develop myocarditis or pericarditis **after** receipt of the first dose of an mRNA COVID-19 vaccine but **before** administration of a subsequent dose:*

- Unclear if there is increased risk of further adverse cardiac effects following a second dose
- Until additional safety data are available, defer receiving a subsequent dose
- Can consider administration of a second dose in certain circumstances
  - Personal risk of severe acute COVID-19 (e.g., age, underlying conditions)
  - Level of COVID-19 community transmission and personal risk of infection
  - Availability of additional data on
    - Risk of myocarditis or pericarditis following an occurrence of either condition after a dose
    - Long-term outcomes of myocarditis or pericarditis after receipt of an mRNA COVID-19 vaccine
  - Timing of any immunomodulatory therapies[1]

[1]ACIP's general best practice guidelines for immunization can be consulted for more information.

Considerations for use of mRNA COVID-19 vaccines in people with a history of myocarditis or pericarditis (2)

People with a history of myocarditis or pericarditis prior to vaccination OR people who choose to receive a subsequent dose of an mRNA COVID-19 vaccine following an occurrence of myocarditis or pericarditis after receipt of a dose should:

- Wait at least until an episode of myocarditis or pericarditis has completely resolved:
  - Including all symptoms attributed to myocarditis or pericarditis
  - No evidence of ongoing heart inflammation or sequelae as determined by the person's clinical team, which may include a cardiologist, and special testing to completely assess cardiac recovery
- Decisions about proceeding with vaccination should include a conversation between the patient, their parent, guardian, or caregiver (as relevant), and their clinical team.
- Clinicians should consult current clinical guidance for information on the evaluation and management of myocarditis.

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html

Guillain-Barré syndrome after vaccination with Janssen COVID-19 Vaccine

- Guillain-Barré syndrome (GBS) is a neurological disorder in which the body's immune system damages nerve cells, causing muscle weakness and sometimes paralysis.
- Reports of adverse events following use of Janssen COVID-19 Vaccine suggest an increased risk of GBS during the 42 days following vaccination.
- No increased risk of GBS identified with mRNA vaccines during use under EUA.
- ACIP's General Best Practice Guidelines for Immunization do not identify a history of GBS as a contraindication to vaccination; GBS is a precaution for influenza vaccines and tetanus-toxoid containing vaccines in limited situations.[1]

[1]In a post-marketing observational study of people vaccinated with Shingrix (for prevention of herpes zoster [shingles]), ~3-6 excess GBS cases per 1 million doses administered to persons ≥65 years in the 6 weeks after vaccination were observed. Although a causal relationship has not been established, FDA added a new warning about GBS in the Prescribing Information for Shingrix on March 24, 2021.

Use of Janssen COVID-19 Vaccine after reports of GBS in vaccine recipients

On July 22, 2021, ACIP reviewed a benefit-risk assessment of GBS after vaccination with Janssen COVID-19 Vaccine.

- ACIP reaffirmed its interim recommendation for the use of the Janssen COVID-19 Vaccine in all persons aged ≥18.
- People with a history of GBS can receive any currently FDA-approved or -authorized COVID-19 vaccine.
- Given the possible association between Janssen COVID-19 vaccine and an increased risk of GBS, patients with a history of GBS should discuss the available mRNA COVID-19 vaccines with their clinical team.
- Any occurrence of GBS following COVID-19 vaccination should be reported to VAERS.
- CDC and FDA will continue to monitor and review cases of GBS among people who receive any COVID-19 vaccine authorized or approved by FDA.

Thrombosis with thrombocytopenia syndrome (TTS) after vaccination with Janssen COVID-19 Vaccine

TTS is a rare syndrome that involves acute venous or arterial thrombosis and new onset thrombocytopenia in patients with no recent known exposure to heparin.

- Most people with TTS after Janssen COVID-19 vaccination had clots in cerebral venous sinuses.
- Clots occurred in other unusual locations (e.g., portal vein, splenic vein) and as a combination of venous and arterial thromboses.
- Highest rates of TTS per vaccine doses administered are in women aged 18-49 years.
- Clinicians can consult the April 13, 2021 Health Alert Network (HAN) notification and guidance from the American Society of Hematology for information on diagnosing and treating suspected cases of TTS.

https://emergency.cdc.gov/han/2021/han00442.asp
https://www.hematology.org/covid-19/vaccine-induced-immune-thrombotic-thrombocytopenia

Considerations for use of Janssen COVID-19 Vaccine in certain populations

A review of available data found that Janssen COVID-19 vaccine's known and potential benefits outweigh its known and potential risks.

Women aged <50 years:

- Can receive any COVID-19 vaccine authorized or approved by FDA
- Should be made aware of the rare risk of TTS after the Janssen Vaccine[1] and the availability of other COVID-19 vaccines (i.e., mRNA vaccines)

People with prior episode of an immune-mediated syndrome characterized by thrombosis and thrombocytopenia, such as heparin-induced thrombocytopenia (HIT):[2]

- Should be offered another FDA-authorized or -approved COVID-19 vaccine (i.e., mRNA vaccine) if it has been ≤90 days since their illness resolved
- May be vaccinated with any COVID-19 vaccine authorized or approved by FDA if more than 90 days have passed since their illness resolved

[1]The highest rates of TTS per vaccine doses administered were identified in women <50 years of age

[2]Although the etiology of TTS associated with the Janssen COVID-19 Vaccine is unclear, it appears to be similar to HIT.

Considerations for use of Janssen COVID-19 Vaccine in certain populations (continued)

People with risk factors for venous thromboembolism (VTE):[1]

- Are unlikely to be at increased risk for TTS because the biologic mechanisms for VTE (as well as arterial thrombi) differ from the immune-mediated mechanism for HIT
- Can receive any FDA-approved or authorized vaccine, including Janssen COVID-19 Vaccine

People who are pregnant, in the postpartum period, or take certain hormonal contraceptives:

- Have an increased risk for VTE. However, these factors are not believed to make people more susceptible to TTS after receipt of Janssen COVID-19 Vaccine.
- Can receive any FDA-approved or authorized vaccine, including Janssen COVID-19 Vaccine

People should not take aspirin or an anticoagulant before vaccination with Janssen COVID-19 Vaccine (or any other FDA-approved or -authorized COVID-19 vaccine) unless taken as part of their routine medications.

[1]Risk factors for VTE include inherited or acquired thrombophilia or a prior history of other types of thromboses (including cerebral venous sinus thrombosis not associated with thrombocytopenia)

Considerations involving pregnancy, lactation, and fertility

COVID-19 vaccination is recommended for all people aged ≥12 years, including people who are pregnant, lactating, trying to get pregnant, or who might become pregnant in the future.

Safety

- COVID-19 vaccines do not cause infection in a pregnant or lactating person, fetus, or infant.
- No safety signals have been observed in animal studies.
- Early safety data on mRNA COVID-19 vaccines during pregnancy are reassuring.
- Early data suggest that mRNA COVID-19 vaccines during pregnancy are effective.

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html
https://www.idsociety.org/covid-19-real-time-learning-network/CDC-IDSA-COVID-19-Clinician-Calls/

Considerations involving pregnancy, lactation, and fertility (continued)

COVID-19 vaccination is recommended for all people aged ≥12 years, including people who are pregnant, lactating, trying to get pregnant, or who might become pregnant in the future.

Administration

- Any COVID-19 vaccine approved or authorized by FDA can be administered.
- Pregnant, lactating, and postpartum people aged <50 years should be aware of the rare risk of TTS after Janssen COVID-19 vaccination and the availability of other COVID-19 vaccines.
- There is no evidence that any of the COVID-19 vaccines affect current or future fertility, and routine pregnancy testing is not recommended before receipt of vaccine.
- If a person becomes pregnant following the first dose of a 2-dose mRNA vaccine series, the second dose should be administered as indicated for the person to have maximum protection and to be considered fully vaccinated.

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html
https://www.idsociety.org/covid-19-real-time-learning-network/CDC-IDSA-COVID-19-Clinician-Calls/

Vaccination of children and adolescents

Adolescents aged 12–17 years are eligible to receive the Pfizer-BioNTech COVID-19 Vaccine and may be vaccinated with appropriate consent and assent.

- Follow state and jurisdictional policies and practices for routine immunizations in this age group.
- Available safety, immunogenicity, and reactogenicity data are similar to those seen in young adults aged 16–25 years.
- Syncope (fainting) may occur with injectable vaccines, especially among adolescents.
  - Procedures should be in place to prevent falling injuries and manage syncopal reactions.
  - All people are recommended to be observed for 15 minutes after vaccination.

Children aged <12 years

- Are *not eligible* to receive any FDA-approved or -authorized COVID-19 vaccine.
- Should not receive any COVID-19 vaccine doses (either standard or partial).

https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/pfizer-bioNTech-faqs.html#vaccination-minors
https://www.cdc.gov/vaccinesafety/concerns/fainting.html

Contraindications to COVID-19 vaccination

- Contraindications to vaccination with COVID-19 vaccines
  - Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a component of the COVID-19 vaccine
  - Immediate allergic reaction* of any severity to a previous dose or known (diagnosed) allergy to a component of the vaccine

- People with a contraindication to an mRNA COVID-19 vaccine should not receive a dose of either of the mRNA vaccines (Pfizer-BioNTech or Moderna).
  - People with a contraindication to mRNA COVID-19 vaccines may be able to receive Janssen COVID-19 Vaccine, and vice versa.
  - Known polysorbate allergy is no longer a contraindication to mRNA vaccination but is a contraindication to Janssen COVID-19 Vaccine and a precaution to mRNA COVID-19 vaccination.

*Immediate allergic reaction to a vaccine or medication is defined as any hypersensitivity-related signs or symptoms consistent with urticaria, angioedema, respiratory distress (e.g., wheezing, stridor), or anaphylaxis that occur within four hours following administration.

Precautions to COVID-19 vaccines

People with a history of an immediate reaction to a vaccine or injectable therapy that contains multiple components, one or more of which is a component of a COVID-19 vaccine, have a precaution to vaccination with that COVID-19 vaccine even if it is unknown which component elicited the allergic reaction.

- **Most people deemed to have a precaution to a COVID-19 vaccine at the time of their vaccination appointment *can and should* be administered vaccine.**
- People with a contraindication to one type of currently authorized COVID-19 vaccines (e.g., mRNA) have a precaution to the other (e.g., Janssen viral vector).
  - Consultation with an allergist-immunologist or the Clinical Immunization Safety Assessment COVIDvax should be considered because of the potential for cross-reactive hypersensitivity between COVID-19 vaccines.
  - Vaccination should only be undertaken in an appropriate setting under the supervision of a healthcare provider experienced in the management of severe allergic reactions.

Potential cross-reactive hypersensitivity between COVID-19 vaccines: Polyethylene glycol (PEG) and polysorbate

PEG and polysorbate are structurally related, and cross-reactive hypersensitivity between these compounds may occur.

- PEG is an ingredient in both mRNA COVID-19 vaccines.
- Polysorbate 80 is an ingredient in Janssen COVID-19 Vaccine.

Post-vaccination symptoms

Before vaccination, providers should counsel vaccine recipients about expected local and systemic post-vaccination symptoms.

Although reactions vary by vaccine product, age group, and dose, symptoms generally:

- Occur during the 7 days after vaccination, usually within the first 3 days
- Are mild to moderate in severity
- Resolve within 1-3 days of onset
- Occur more frequently and with greater severity:
  - Following the second dose
  - Among younger age groups

https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/reactogenicity.html
https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/reactogenicity.html
https://www.cdc.gov/vaccines/covid-19/info-by-product/janssen/reactogenicity.html

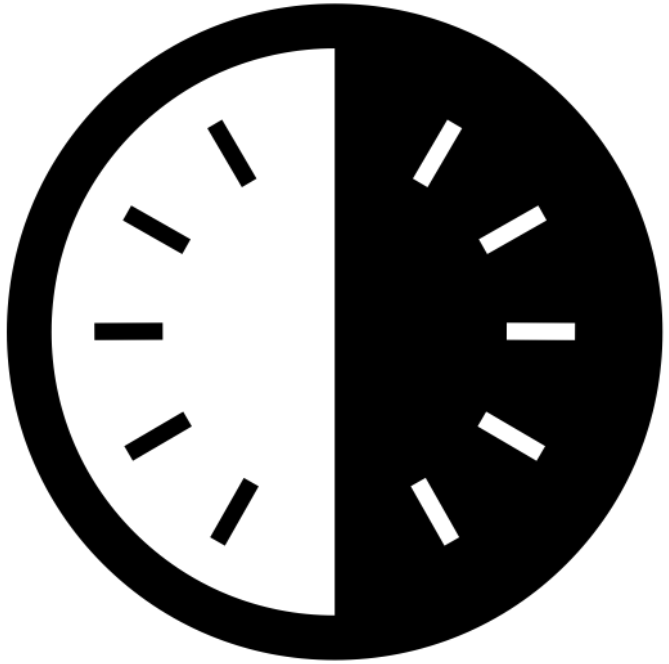
Delayed-onset local reactions to 1st dose of COVID-19 vaccine

- Delayed-onset local reactions (e.g., erythema, induration, pruritus around the injection site area) beginning a few days through the second week after the first dose are **not** a contraindication or precaution to receiving a second dose.
- Whether persons who experienced a delayed-onset injection site reaction after the first dose will experience a similar reaction after the second dose is unknown. However, such reactions are believed not to represent a risk for anaphylaxis upon receipt of the second dose.
- Persons with delayed injection site reactions after the first mRNA COVID-19 vaccine dose should receive a second dose of the same vaccine product at the recommended interval, **preferably in the opposite arm**.

Observation period following vaccination

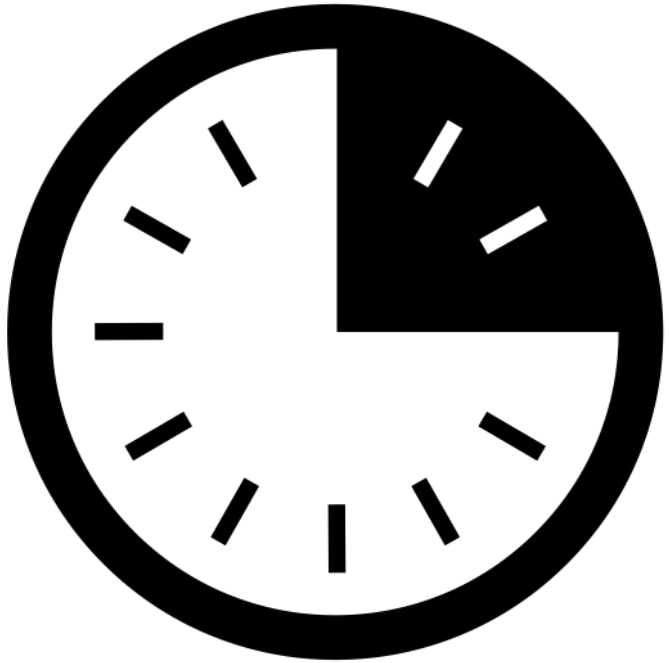
30 minutes

- History of immediate allergic reaction to a vaccine or injectable therapy
- Contraindication to a different type of COVID-19 vaccine
- History of anaphylaxis from any cause



15 minutes

- All other people



Triage of people presenting for COVID-19 vaccination

CONTRAINDICATION TO VACCINATION

History of the following:

- Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to component of the vaccine†
- Immediate allergic reaction* of any severity after a previous dose or known (diagnosed) allergy to a component of the vaccine†

Actions

- Do not vaccinate.
- Consider referral to allergist-immunologist.
- Consider other vaccine alternative.†

PRECAUTION TO VACCINATION

Among people without a contraindication, a history of:

- Any immediate allergic reaction* to other vaccines or injectable therapies‡

Note: people with a contraindication to mRNA COVID-19 vaccines have a precaution to Janssen COVID-19 vaccine, and vice versa. See footnote for additional information on additional measures to take in these people.#

Actions

- Risk assessment
- Consider referral to allergist-immunologist
- 30-minute observation period if vaccinated

MAY PROCEED WITH VACCINATION

Among people without a contraindication or precaution, a history of:

- Allergy to oral medications (including the oral equivalent of an injectable medication)
- History of food, pet, insect, venom, environmental, latex, etc., allergies
- Family history of allergies

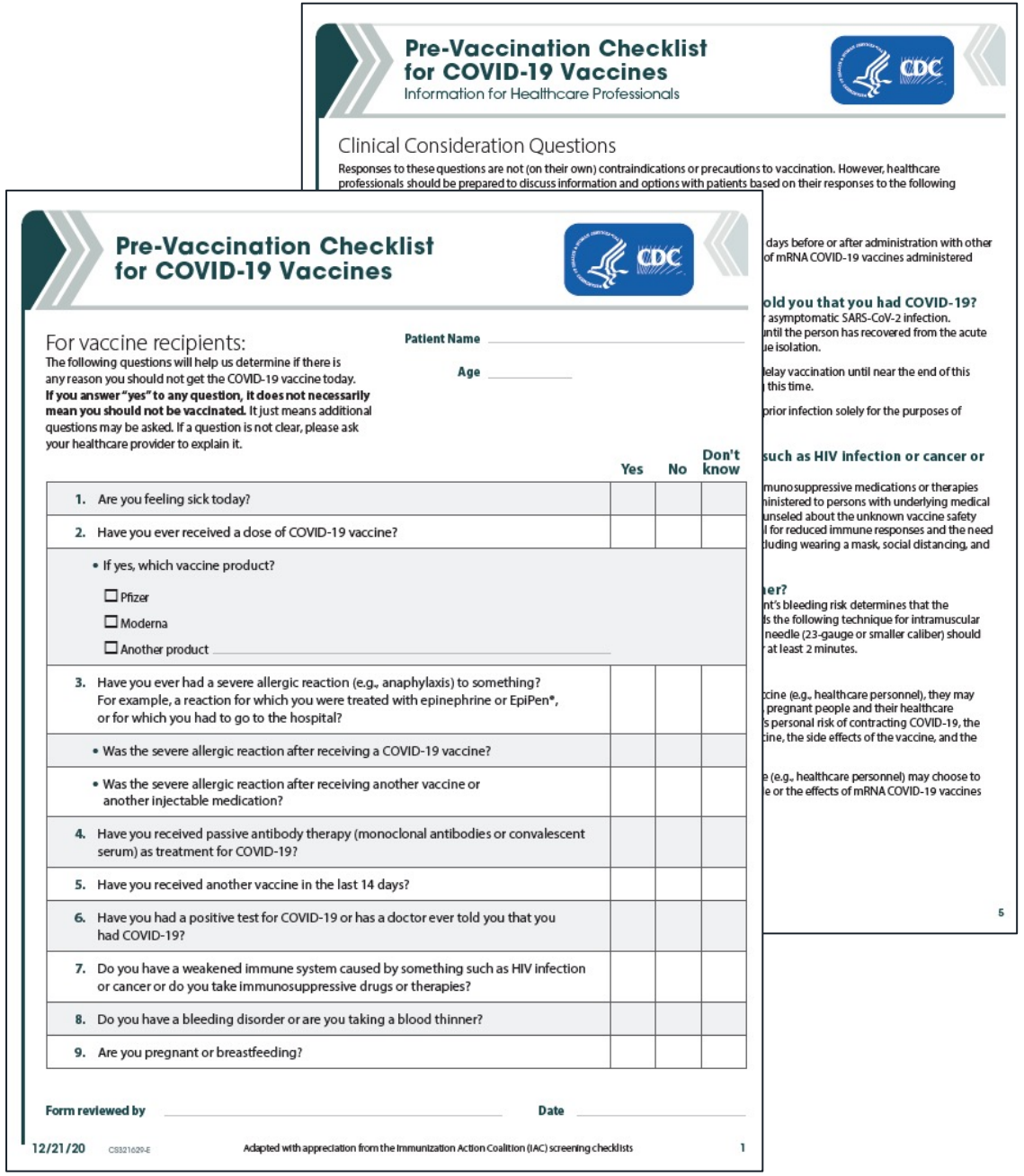
Actions

- 30-minute observation period: People with a history of anaphylaxis (due to any cause)
- 15-minute observation period: All other people

† See Appendix C for a list of ingredients. People with a contraindication to one of the mRNA COVID-19 vaccines should not receive doses of either of the mRNA vaccines (Pfizer-BioNTech or Moderna).
* Immediate allergic reaction to a vaccine or medication is defined as any hypersensitivity-related signs or symptoms consistent with urticaria, angioedema, respiratory distress (e.g., wheezing, stridor), or anaphylaxis that occur within four hours following administration.
‡People with a history of an immediate reaction to a vaccine or injectable therapy that contains multiple components, one or more of which is a component of a COVID-19 vaccine, have a precaution to vaccination with that COVID-19 vaccine even if it is unknown which component elicited the allergic reaction.
#Polyethylene glycol (PEG) is an ingredient in both mRNA COVID-19 vaccines, and polysorbate 80 is an ingredient in Janssen COVID-19 vaccine. PEG and polysorbate are structurally related, and cross-reactive hypersensitivity between these compounds may occur. People with a contraindication to mRNA COVID-19 vaccines (including due to a known allergy to PEG) have a precaution to Janssen COVID-19 vaccine. Among people who received one mRNA COVID-19 dose but for whom the second dose is contraindicated, consideration may be given to vaccination with Janssen COVID-19 vaccine (administered at least 28 days after the mRNA COVID-19 dose). People with a contraindication to Janssen COVID-19 vaccine (including due to a known allergy to polysorbate) have a precaution to mRNA COVID-19 vaccines. In patients with these precautions, referral to an allergist-immunologist should be considered. Healthcare providers and health departments may also request a consultation from the Clinical Immunization Safety Assessment COVIDvax project. In patients with these precautions, vaccination should only be undertaken in an appropriate setting under the supervision of a health care provider experienced in the management of severe allergic reactions.

Additional tools

To identify people with contraindications and precautions to vaccination



Pre-Vaccination Checklist for COVID-19 Vaccines

Information for Healthcare Professionals

Clinical Consideration Questions

Responses to these questions are not (on their own) contraindications or precautions to vaccination. However, healthcare professionals should be prepared to discuss information and options with patients based on their responses to the following

Pre-Vaccination Checklist for COVID-19 Vaccines

For vaccine recipients:

The following questions will help us determine if there is any reason you should not get the COVID-19 vaccine today. **If you answer "yes" to any question, it does not necessarily mean you should not be vaccinated.** It just means additional questions may be asked. If a question is not clear, please ask your healthcare provider to explain it.

Patient Name _____

Age _____

	Yes	No	Don't know
1. Are you feeling sick today?			
2. Have you ever received a dose of COVID-19 vaccine?			
• If yes, which vaccine product? ☐ Pfizer ☐ Moderna ☐ Another product _____			
3. Have you ever had a severe allergic reaction (e.g., anaphylaxis) to something? For example, a reaction for which you were treated with epinephrine or EpiPen®, or for which you had to go to the hospital?			
• Was the severe allergic reaction after receiving a COVID-19 vaccine?			
• Was the severe allergic reaction after receiving another vaccine or another injectable medication?			
4. Have you received passive antibody therapy (monoclonal antibodies or convalescent serum) as treatment for COVID-19?			
5. Have you received another vaccine in the last 14 days?			
6. Have you had a positive test for COVID-19 or has a doctor ever told you that you had COVID-19?			
7. Do you have a weakened immune system caused by something such as HIV infection or cancer or do you take immunosuppressive drugs or therapies?			
8. Do you have a bleeding disorder or are you taking a blood thinner?			
9. Are you pregnant or breastfeeding?			

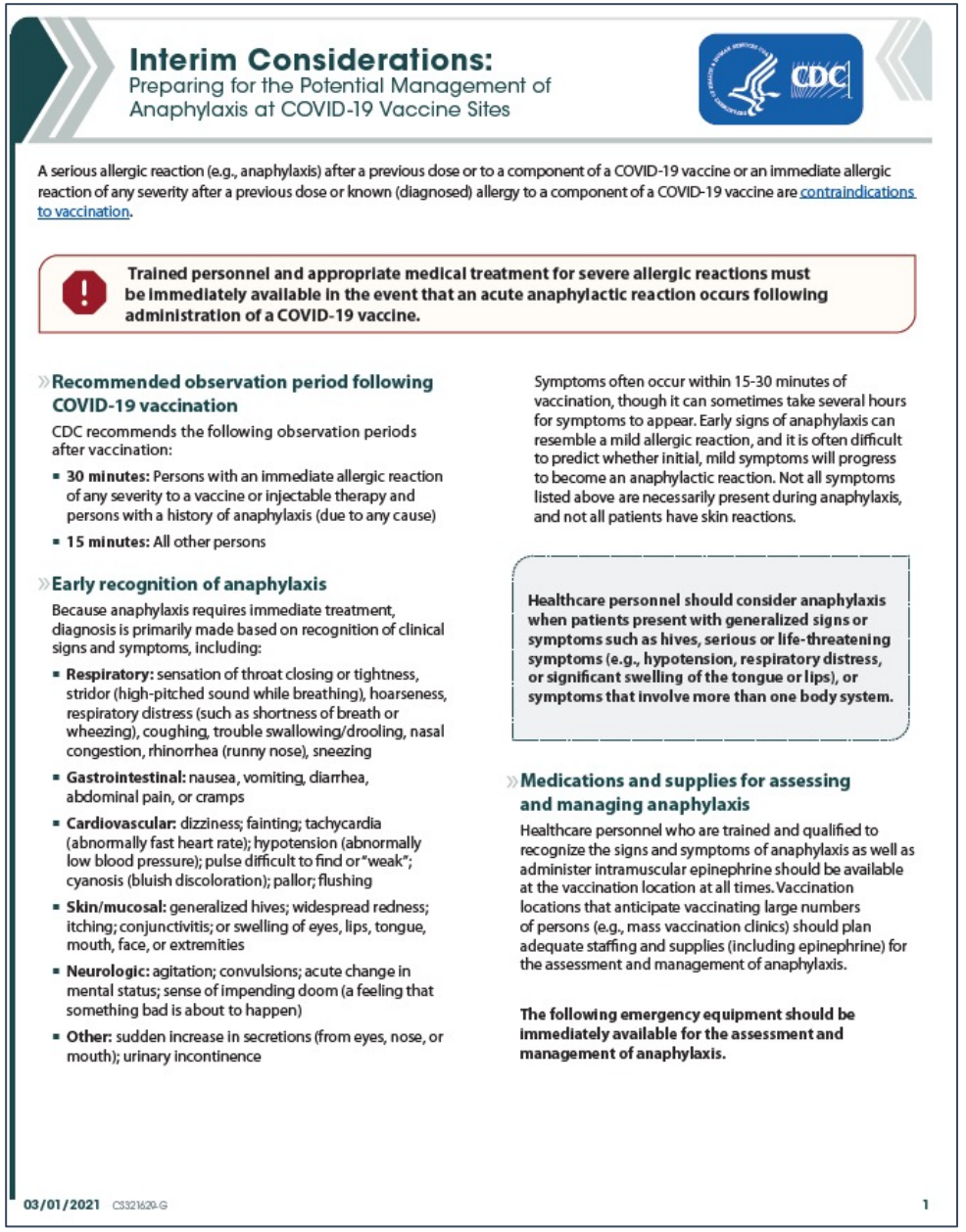
Form reviewed by _____ Date _____

12/21/20 CS321629-E Adapted with appreciation from the Immunization Action Coalition (IAC) screening checklists 1

https://www.cdc.gov/vaccines/covid-19/downloads/pre-vaccination-screening-form.pdf

Additional tools

Preparing for the potential management of anaphylaxis at COVID-19 vaccination sites



Interim Considerations:
Preparing for the Potential Management of Anaphylaxis at COVID-19 Vaccine Sites

A serious allergic reaction (e.g., anaphylaxis) after a previous dose or to a component of a COVID-19 vaccine or an immediate allergic reaction of any severity after a previous dose or known (diagnosed) allergy to a component of a COVID-19 vaccine are contraindications to vaccination.

Trained personnel and appropriate medical treatment for severe allergic reactions must be immediately available in the event that an acute anaphylactic reaction occurs following administration of a COVID-19 vaccine.

Recommended observation period following COVID-19 vaccination

CDC recommends the following observation periods after vaccination:

- **30 minutes:** Persons with an immediate allergic reaction of any severity to a vaccine or injectable therapy and persons with a history of anaphylaxis (due to any cause)
- **15 minutes:** All other persons

Early recognition of anaphylaxis

Because anaphylaxis requires immediate treatment, diagnosis is primarily made based on recognition of clinical signs and symptoms, including:

- **Respiratory:** sensation of throat closing or tightness, stridor (high-pitched sound while breathing), hoarseness, respiratory distress (such as shortness of breath or wheezing), coughing, trouble swallowing/drooling, nasal congestion, rhinorrhea (runny nose), sneezing
- **Gastrointestinal:** nausea, vomiting, diarrhea, abdominal pain, or cramps
- **Cardiovascular:** dizziness; fainting; tachycardia (abnormally fast heart rate); hypotension (abnormally low blood pressure); pulse difficult to find or "weak"; cyanosis (bluish discoloration); pallor; flushing
- **Skin/mucosal:** generalized hives; widespread redness; itching; conjunctivitis; or swelling of eyes, lips, tongue, mouth, face, or extremities
- **Neurologic:** agitation; convulsions; acute change in mental status; sense of impending doom (a feeling that something bad is about to happen)
- **Other:** sudden increase in secretions (from eyes, nose, or mouth); urinary incontinence

Symptoms often occur within 15-30 minutes of vaccination, though it can sometimes take several hours for symptoms to appear. Early signs of anaphylaxis can resemble a mild allergic reaction, and it is often difficult to predict whether initial, mild symptoms will progress to become an anaphylactic reaction. Not all symptoms listed above are necessarily present during anaphylaxis, and not all patients have skin reactions.

Healthcare personnel should consider anaphylaxis when patients present with generalized signs or symptoms such as hives, serious or life-threatening symptoms (e.g., hypotension, respiratory distress, or significant swelling of the tongue or lips), or symptoms that involve more than one body system.

Medications and supplies for assessing and managing anaphylaxis

Healthcare personnel who are trained and qualified to recognize the signs and symptoms of anaphylaxis as well as administer intramuscular epinephrine should be available at the vaccination location at all times. Vaccination locations that anticipate vaccinating large numbers of persons (e.g., mass vaccination clinics) should plan adequate staffing and supplies (including epinephrine) for the assessment and management of anaphylaxis.

The following emergency equipment should be immediately available for the assessment and management of anaphylaxis.

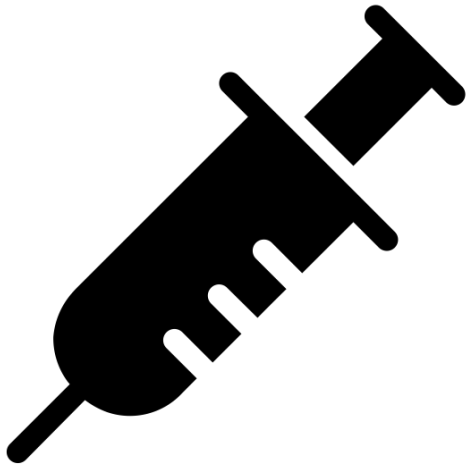
03/01/2021 CS321629-G 1

https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/anaphylaxis-management.html

Preparing for the potential management of anaphylaxis at COVID-19 vaccination sites

Early recognition of anaphylaxis symptoms

Prompt treatment with epinephrine



Activation of emergency medical services

https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/anaphylaxis-management.html

Vaccination and use of immune-based tests for tuberculosis

- COVID-19 vaccination should not be delayed because of testing for tuberculosis (TB) infection.

- Testing for TB infection with tuberculin skin test (TST) or an interferon release assay (IGRA) can be done before, after, or during the encounter for COVID-19 vaccination.

https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/reactogenicity.html
https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/reactogenicity.html
https://www.cdc.gov/vaccines/covid-19/info-by-product/janssen/reactogenicity.html

Additional Resources

CDC Resources

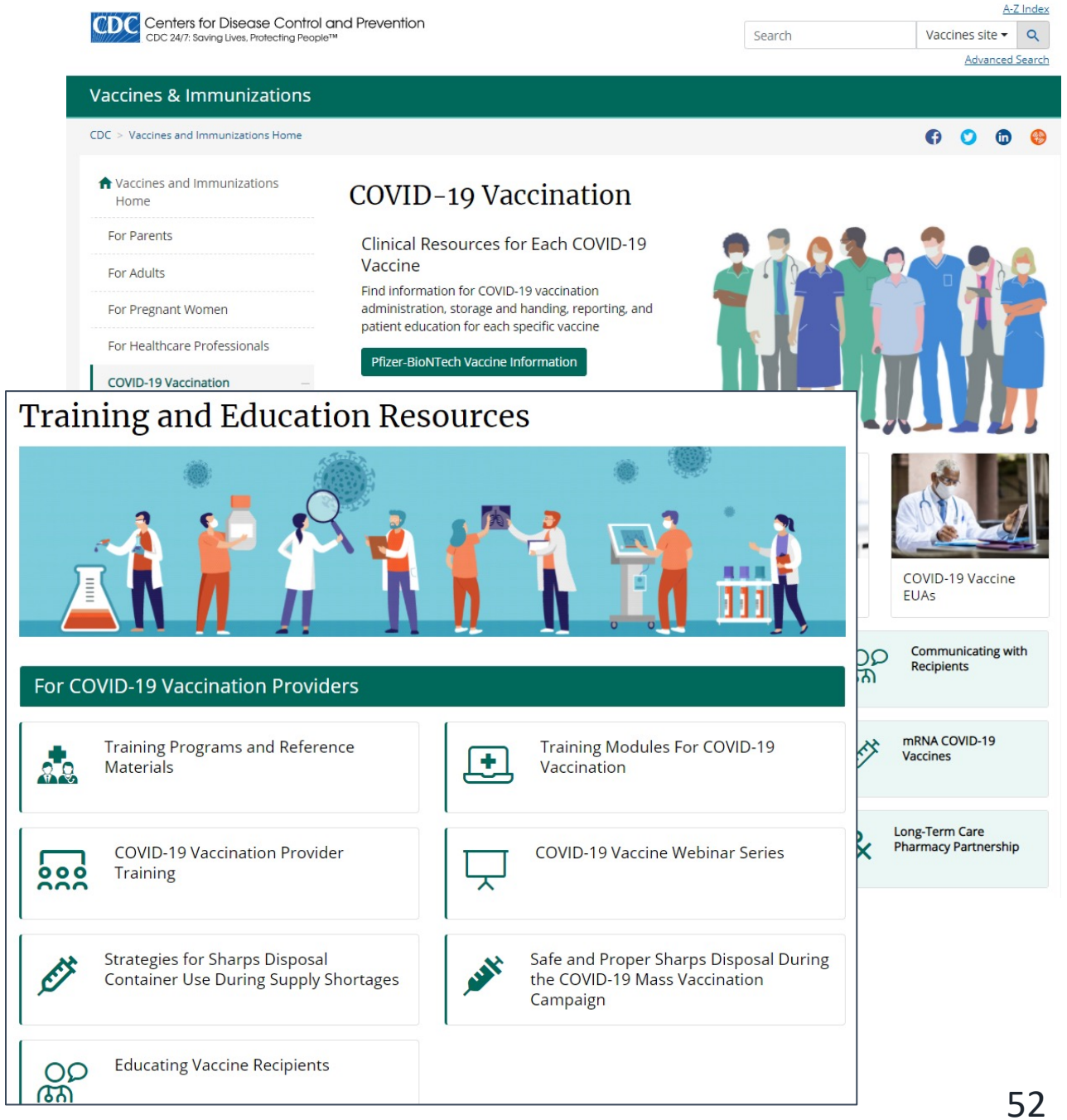
Learn more with **CDC's COVID-19 vaccine tools and resources.** Find information for COVID-19 vaccination administration, storage, reporting, patient education, and more.

COVID-19 vaccination resources for healthcare professionals

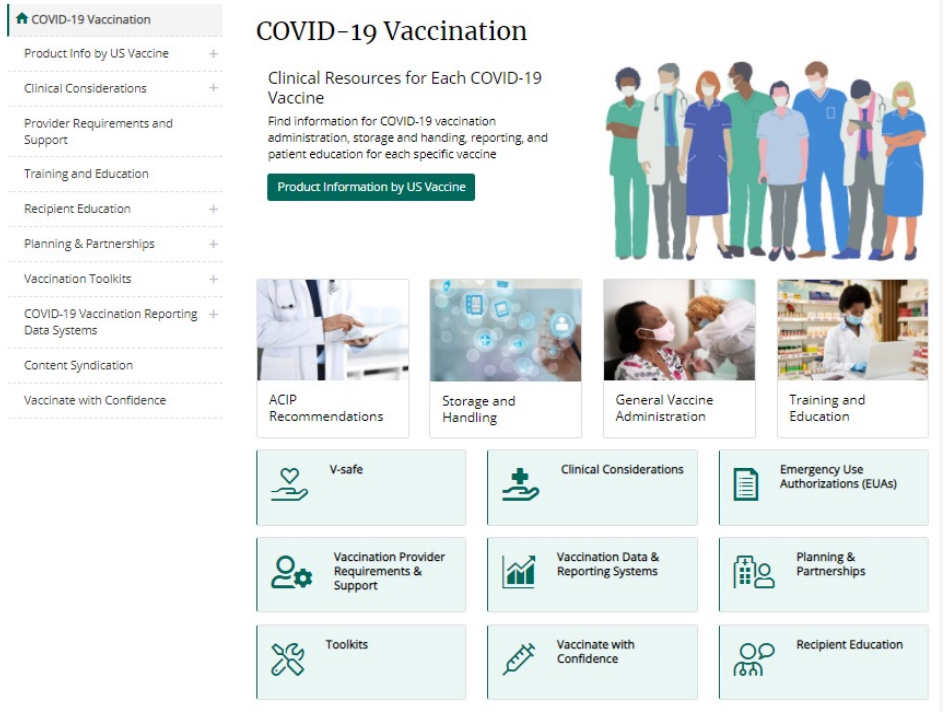
www.cdc.gov/vaccines/covid-19/index.html

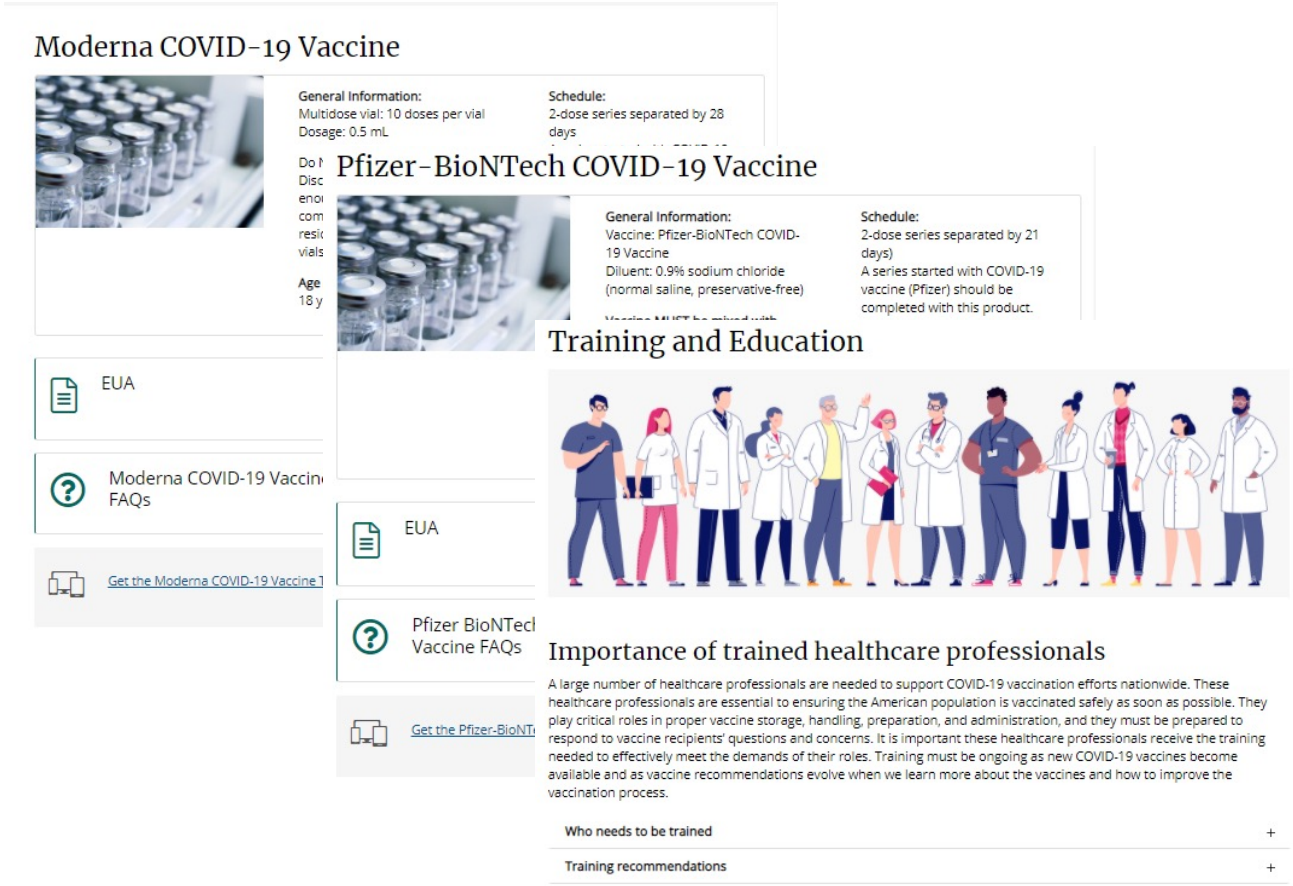
For healthcare professionals
www.cdc.gov/vaccines/covid-19/hcp/index.html

Healthcare infection prevention and control recommendations after COVID-19 vaccination
www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-after-vaccination.html



CDC COVID-19 vaccine clinical trainings and materials





www.cdc.gov/vaccines/covid-19/index.html
www.cdc.gov/vaccines/covid-19/info-by-product/index.html
www.cdc.gov/vaccines/covid-19/training-education/index.html
www.cdc.gov/vaccines/covid-19/training-education/resources.html

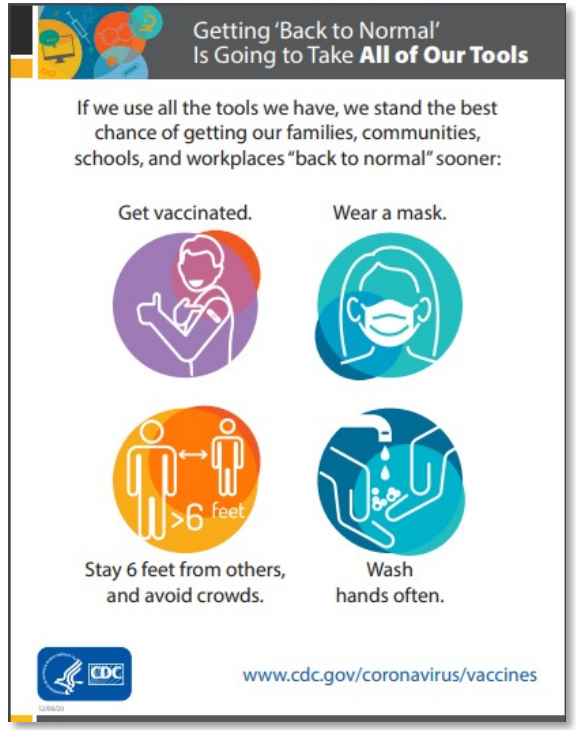
COVID-19 vaccine communication resources

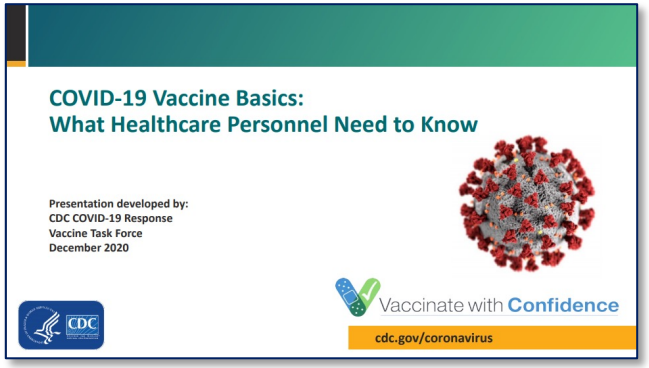
Engaging in effective COVID-19 vaccine conversations
https://www.cdc.gov/vaccines/covid-19/hcp/engaging-patients.html

COVID-19 vaccination toolkits are available for

- Medical centers, clinics, and clinicians
- Pediatric healthcare professionals
- Long-term care facilities
- Health departments
- Community-based organizations
- Essential workers
- Staff in school settings and childcare programs

- www.cdc.gov/vaccines/covid-19/health-systems-communication-toolkit.html
- www.cdc.gov/coronavirus/2019-ncov/vaccines/toolkits.html





Reporting of vaccine adverse events

- Adverse events in COVID-19 vaccine recipients are required to be reported to VAERS.*
- FDA's COVID-19 vaccine EUAs and EUA/BLA require vaccination providers to report
  - Vaccine administration errors
  - Serious adverse events
  - Cases of multisystem inflammatory syndrome
  - Cases of COVID-19 that result in hospitalization or death

  Reporting is encouraged for all other clinically significant adverse events, even those not clearly attributable to vaccination.

*Instructions for submitting a report to VAERS is available at https://vaers.hhs.govexternal or by calling 1-800-822-7967.

Active Safety Monitoring for COVID-19 Vaccines

v-safe is a new CDC smartphone-based monitoring program for COVID-19 vaccine safety:

- Uses text messaging and web surveys to check in with vaccine recipients after vaccination
- Participants can report any side effects or health problems after COVID-19 vaccination.
- Parents/guardians can enroll adolescents (ages ≥12 years) in v-safe and complete health check-ins on their behalf.
- Includes active telephone follow-up by CDC for reports of significant health impact

v-safe COVID-19 Vaccine Pregnancy Registry collects additional health information from v-safe participants who report being pregnant at the time of vaccination or a positive pregnancy test after vaccination.

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafe.html

Clinical Considerations: Appendix A

How to manage vaccine administration errors and deviations

https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html#Appendix-A

Appendix A. Vaccine administration errors and deviations

A vaccine administration error is any preventable event that may cause or lead to inappropriate use of vaccine or patient harm. This appendix provides resources for preventing and reporting mRNA COVID-19 vaccine administration errors, as well as actions to take after an error has occurred. For completeness, this includes additional scenarios that deviate from CDC recommendations for vaccine intervals but are not considered administration errors. This document is intended to assist providers with handling exceptional situations in which a vaccination error or deviation has already occurred and may be updated when additional information becomes available.

The FDA-issued Emergency Use Authorization and Fact Sheet for Healthcare Providers Administering Vaccines should be referenced for detailed information on storage and handling, dosing and schedule, dose preparation, and administration of mRNA COVID-19 vaccines. The information provided below on managing vaccine administration errors should not be interpreted as a recommendation or promotion of unauthorized use of the vaccines.

For all vaccine administration errors:

- Inform the recipient of the vaccine administration error.
- Consult with the state immunization program and/or Immunization Information System (IIS) to determine how the dose should be entered into the IIS, both as an administered dose and to account for inventory.
- Report the error to the Vaccine Adverse Event Reporting System (VAERS), unless otherwise indicated in the table. Providers are required to report all COVID-19 vaccine administration errors—even those not associated with an adverse event — to the VAERS. To file an electronic report, please see the VAERS website .
- Determine how the error occurred and implement strategies to prevent it from happening again. A discussion on strategies to prevent errors can be found in the Vaccine Administration chapter of the *Epidemiology and Prevention of Vaccine-Preventable Diseases* (Pink Book). Additional resources can be found on CDC's vaccine administration web page, including a job aid for preventing errors.

Type	Administration error/deviation	Interim recommendation
Site/route	• Incorrect site (i.e., site other than the deltoid muscle [preferred site] or anterolateral thigh [alternate site])	• Do **not** repeat dose.*
	• Incorrect route (e.g., subcutaneous)	• Do **not** repeat dose.*
Age	• Unauthorized age group	• If received first dose at age less than 16 years, do not give second dose at this time∞. • If age 16 to 17 years and Moderna vaccine inadvertently administered instead of Pfizer-BioNTech as the first dose, may administer Moderna vaccine as the second dose (as off-label use, because Moderna vaccine is not authorized in this age group).
Intervals	• Second dose administered fewer than 17 days (Pfizer-BioNTech) or fewer than 24 days (Moderna) after the first dose (i.e., administered earlier than the 4-day grace period)	• Do **not** repeat dose.