Interim Clinical Considerations for Use of mRNA COVID-19 Vaccines | CDC

Summary of recent changes (last updated February 10, 2021):

- New recommendations for preventing, reporting, and managing mRNA COVID-19 vaccine administration errors (Appendix A).
- Clarification on contraindications and precautions. Persons with a known (diagnosed) allergy to PEG, another mRNA vaccine component, or polysorbate, have a contraindication to vaccination. Persons with a reaction to a vaccine or injectable therapy that contains multiple components, one of which is PEG, another mRNA vaccine component or polysorbate, but in whom it is unknown which component elicited the immediate allergic reaction have a precaution to vaccination.
- Updated information on delayed, local injection-site reactions after the first mRNA vaccine dose. These reactions are neither a contraindication or precaution to the second dose.
- Updated quarantine recommendations for vaccinated persons. Fully vaccinated persons who meet criteria will no longer be required to quarantine following an exposure to someone with COVID-19. Additional considerations for patients and residents in healthcare settings are provided.
- Additional information and updated recommendations for testing for TB infection. TB testing can be done before or at the same time as mRNA COVID-19 vaccination, or otherwise delayed for ≥4 weeks after the completion of mRNA COVID-19 vaccination.

Background

The Advisory Committee on Immunization Practices (ACIP) has issued interim recommendations for the use of Pfizer-BioNTech and Moderna COVID-19 vaccines for the prevention of coronavirus disease 2019 (COVID-19) in the United States. Both vaccines are lipid nanoparticle-formulated, nucleoside-modified mRNA vaccines encoding the prefusion spike glycoprotein of SARS-CoV-2, the virus that causes COVID-19.

These interim CDC clinical considerations are informed by data submitted to the Food and Drug Administration (FDA) for Emergency Use Authorization (EUA) of the vaccines, other data sources, general best practice guidelines for immunization, and expert opinion. These considerations for mRNA vaccines only apply to the currently authorized vaccine products in the United States (i.e., Pfizer-BioNTech and Moderna COVID-19 vaccines). Considerations will be updated when additional information becomes available and/or if additional vaccine products are authorized.

In addition to the following considerations, the EUA conditions of use and storage, handling, and administration procedures described in the prescribing information should be referenced when using the Pfizer-BioNTech and Moderna COVID-19 vaccines.

Authorized age groups

Under the EUAs, the following age groups are authorized to receive vaccination:

- Pfizer-BioNTech: ages ≥16 years

- Moderna: ages ≥18 years

Children and adolescents outside of these authorized age groups should not receive COVID-19 vaccination at this time.

Administration

The mRNA COVID-19 vaccine series consist of two doses administered intramuscularly:

- Pfizer-BioNTech (30 µg, 0.3 ml each): 3 weeks (21 days) apart
- Moderna (100 µg, 0.5 ml): 1 month (28 days) apart

Persons should not be scheduled to receive the second dose earlier than recommended (i.e., 3 weeks [Pfizer-BioNTech] or 1 month [Moderna]). However, second doses administered within a grace period of 4 days earlier than the recommended date for the second dose are still considered valid. Doses inadvertently administered earlier than the grace period should not be repeated.

The second dose should be administered as close to the recommended interval as possible. However, if it is not feasible to adhere to the recommended interval and a delay in vaccination is unavoidable, the second dose of Pfizer-BioNTech and Moderna COVID-19 vaccines may be administered up to 6 weeks (42 days) after the first dose. There are currently limited data on efficacy of mRNA COVID-19 vaccines administered beyond this window. If the second dose is administered beyond these intervals, there is no need to restart the series.

Information on preventing, reporting, and managing mRNA COVID-19 vaccine administration errors is found in Appendix A. Vaccine

administration errors should be reported to the Vaccine Adverse Event Reporting System (VAERS).

Interchangeability with other COVID-19 vaccine products

Either of the currently authorized mRNA COVID-19 vaccines can be used when indicated; ACIP does not state a product preference. However, **these mRNA COVID-19 vaccines are not interchangeable with each other or with other COVID-19 vaccine products**. The safety and efficacy of a mixed-product series have not been evaluated. Both doses of the series should be completed with the same product.

Strategies to help ensure that patients receive the second dose with the appropriate product and interval between doses include:

- Providing COVID-19 vaccination record cards to vaccine recipients, asking recipients to bring their card to their appointment for the second dose, and encouraging recipients to make a backup copy (e.g., by taking a picture of the card on their phone).
- Encouraging vaccine recipients to enroll in VaxText^{SM}, a free text message-based platform to receive COVID-19 vaccination second-dose reminders.
- Recording each recipient's vaccination in the immunization information system (IIS).
- Recording vaccine administration information in the patient's medical record.
- Making an appointment for the second dose before the vaccine recipient leaves, to increase the likelihood that patients will present at the same vaccination site for the second dose.

Using the above strategies, every effort should be made to determine which vaccine product was received as the first dose, in order to ensure completion of the vaccine series with the same product. In exceptional situations in which the first-dose vaccine product cannot be determined or is no longer available, any available mRNA COVID-19 vaccine may be administered at a minimum interval of 28 days between doses to complete the mRNA COVID-19 vaccination series. If two doses of different mRNA COVID-19 vaccine products are administered in these situations (or inadvertently), no additional doses of either product are recommended at this time.

Recommendations may be updated when further information becomes available or other vaccine types (e.g., viral vector, protein subunit vaccines) are authorized.

Coadministration with other vaccines

Given the lack of data on the safety and efficacy of mRNA COVID-19 vaccines administered simultaneously with other vaccines, the vaccine series should routinely be administered alone, with a minimum interval of 14 days before or after administration with any other vaccine. However, mRNA COVID-19 and other vaccines may be administered within a shorter period in situations where the benefits of vaccination are deemed to outweigh the potential unknown risks of vaccine coadministration (e.g., tetanus toxoid-containing vaccination as part of wound management, rabies vaccination for post-exposure prophylaxis, measles or hepatitis A vaccination during an outbreak) or to avoid barriers or delays to mRNA COVID-19 vaccination (e.g., in long-term care facility residents or healthcare personnel who received influenza or other vaccinations prior to/upon admission or onboarding). If mRNA

COVID-19 vaccines are administered within 14 days of another vaccine, doses do not need to be repeated for either vaccine.

Booster doses

The need for and timing of booster doses for mRNA COVID-19 vaccines has not been established. No additional doses beyond the two-dose primary series are recommended at this time.

Vaccination of persons with a SARS-CoV-2 infection or exposure

Persons with a current or prior history of SARS-CoV-2 infection

Data from clinical trials indicate that mRNA COVID-19 vaccines can safely be given to persons with evidence of a prior SARS-CoV-2 infection. Vaccination should be offered to persons regardless of history of prior symptomatic or asymptomatic SARS-CoV-2 infection. Viral testing to assess for acute SARS-CoV-2 infection or serologic testing to assess for prior infection for the purposes of vaccine decision-making is **not** recommended.

Vaccination of persons with known current SARS-CoV-2 infection should be deferred until the person has recovered from the acute illness (if the person had symptoms) and criteria have been met for them to discontinue isolation. This recommendation applies to persons who experience SARS-CoV-2 infection before receiving any vaccine doses as well as those who experience SARS-CoV-2 infection after the first dose but before receipt of the second dose.

While there is no recommended minimum interval between infection

and vaccination, current evidence suggests that the risk of SARS-CoV-2 reinfection is low in the months after initial infection but may increase with time due to waning immunity. Thus, **while vaccine supply remains limited**, persons with recent documented acute SARS-CoV-2 infection may choose to temporarily delay vaccination, if desired, recognizing that the risk of reinfection, and therefore the need for vaccination, might increase with time following initial infection.

For vaccinated persons who subsequently experience COVID-19, prior receipt of an mRNA 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.

Persons who previously received passive antibody therapy

Currently, there are no data on the safety and efficacy of mRNA COVID-19 vaccines in persons who received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment. Based on the estimated half-life of such therapies and evidence suggesting that reinfection is uncommon in the 90 days after initial infection, vaccination should be deferred for at least 90 days, as a precautionary measure until additional information becomes available, to avoid potential interference of the antibody therapy with vaccine-induced immune responses. This recommendation applies to persons who receive passive antibody therapy before receiving any vaccine doses and those who receive passive antibody therapy after the first dose but before the second dose, in which case the second dose should be deferred for at least 90 days following receipt of the antibody therapy.

For persons receiving antibody therapies not specific to COVID-19

treatment (e.g., intravenous immunoglobulin, RhoGAM), administration of mRNA COVID-19 vaccines either simultaneously with or at any interval before or after receipt of an antibody-containing product is unlikely to substantially impair development of a protective antibody response. Thus, there is no recommended minimum interval between other antibody therapies (i.e., those that are not specific to COVID-19 treatment) and mRNA COVID-19 vaccination.

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

mRNA vaccines are not currently recommended for outbreak management or for post-exposure prophylaxis, which is vaccination to prevent the development of SARS-CoV-2 infection in a person with a specific known exposure. Because the median incubation period of SARS-CoV-2 is 4–5 days, it is unlikely that the first dose of COVID-19 vaccine would provide an adequate immune response within the incubation period for effective post-exposure prophylaxis. Thus, vaccination is unlikely to be effective in preventing disease following an exposure.

Persons in the community or outpatient setting who have had a known COVID-19 exposure should not seek vaccination until their quarantine period has ended to avoid potentially exposing healthcare personnel and other persons to SARS-CoV-2 during the vaccination visit.

Residents with a known COVID-19 exposure living in congregate healthcare settings (e.g., long-term care facilities), where exposure and transmission of SARS-CoV-2 can occur repeatedly for long periods of time, may be vaccinated. In these settings, healthcare personnel are already in close contact with residents (e.g., entering patient rooms for

evaluation and treatment). Vaccinators should employ appropriate infection prevention and control procedures.

Residents of other congregate settings (e.g., correctional and detention facilities, homeless shelters) with a known COVID-19 exposure may also be vaccinated, in order to avoid delays and missed opportunities for vaccination given the increased risk for outbreaks in these settings. However, where feasible, precautions should be taken to limit mixing exposed individuals with other residents or staff (except those essential for the provision of vaccination services, who should employ appropriate infection and control procedures).

Persons residing in congregate settings (healthcare and non-healthcare) who have had an exposure and are awaiting results of SARS-CoV-2 testing may be vaccinated if the person does not have symptoms consistent with COVID-19.

In situations where facility-wide testing is being conducted to identify SARS-CoV-2 infections, facilities should attempt to complete facility-wide testing within a period that allows for test results to be received prior to vaccination in order to isolate those patients with SARS-CoV-2 infection. However, it is not necessary to wait for test results if this would create delays in vaccination. In such situations, persons without symptoms consistent with COVID-19 may be vaccinated. Although not contraindicated, vaccination may be deferred pending outcome of testing in persons with symptoms consistent with COVID-19. Viral testing for acute SARS-CoV-2 infection solely for the purposes of vaccine decision-making is not recommended.

Vaccination of persons with underlying medical conditions

mRNA COVID-19 vaccines can administered to persons with underlying medical conditions who have no contraindications to vaccination (see 'contraindications' section below). Clinical trials demonstrated similar safety and efficacy profiles in persons with some underlying medical conditions, including those that place them at increased risk for severe COVID-19, compared to persons without comorbidities. Information on groups with specific underlying medical conditions is included below.

Immunocompromised persons

Persons with HIV infection or other immunocompromising conditions, or who take immunosuppressive medications or therapies might be at increased risk for severe COVID-19. Data are not currently available to establish vaccine safety and efficacy in these groups. Persons with stable HIV infection were included in mRNA COVID-19 vaccine clinical trials, though data remain limited. Immunocompromised individuals can receive COVID-19 vaccination if they have no contraindications to vaccination. However, they should be counseled about the unknown vaccine safety profile and effectiveness in immunocompromised populations, and the potential for reduced immune responses and the need to continue to follow all current guidance to protect themselves against COVID-19 (see below). Antibody testing is not recommended to assess for immunity to COVID-19 following mRNA COVID-19 vaccination.

At this time, re-vaccination is not recommended after immune competence is regained in persons who received mRNA COVID-19 vaccines during chemotherapy or treatment with other immunosuppressive drugs. Recommendations on re-vaccination or additional doses of mRNA COVID-19 vaccines may be updated when additional information is available.

Persons with autoimmune conditions

No data are currently available on the safety and efficacy of mRNA COVID-19 vaccines in persons with autoimmune conditions, though these persons were eligible for enrollment in clinical trials. No imbalances were observed in the occurrence of symptoms consistent with autoimmune conditions or inflammatory disorders in clinical trial participants who received an mRNA COVID-19 vaccine compared to placebo. Persons with autoimmune conditions who have no contraindications to vaccination may receive an mRNA COVID-19 vaccine.

Persons with a history of Guillain-Barré syndrome

To date, no cases of Guillain-Barré syndrome (GBS) have been reported following vaccination among participants in the Pfizer-BioNTech or Moderna COVID-19 vaccines clinical trials. With few exceptions, ACIP's general best practice guidelines for immunization does not include history of GBS as a contraindication or precaution to vaccination. Persons with a history of GBS may receive an mRNA COVID-19 vaccine unless they have a contraindication to vaccination. Any occurrence of GBS following mRNA COVID-19 vaccination should be reported to VAERS.

Persons with a history of Bell's palsy

Cases of Bell's palsy were reported following vaccination in participants in both the Pfizer-BioNTech and Moderna COVID-19 vaccines clinical trials. However, the FDA does not consider these to be above the frequency expected in the general population and has not concluded that these cases were causally related to vaccination. Post-

authorization safety surveillance will be important to further assess any possible causal association. In the absence of such evidence, persons with a history of Bell's palsy can receive an mRNA COVID-19 vaccine unless they have a contraindication to vaccination. Any occurrence of Bell's palsy following mRNA COVID-19 vaccination should be reported to VAERS.

Persons with a history of dermal filler use

Infrequently, persons who have received dermal fillers might experience swelling at or near the site of filler injection (usually face or lips) following administration of a dose of an mRNA COVID-19 vaccine. This appears to be temporary and can resolve with medical treatment, including corticosteroid therapy. mRNA COVID-19 vaccines can be administered to persons who have received injectable dermal fillers who have no contraindications to vaccination (see 'contraindications' section below). No additional precautions are needed. However, these persons should be advised to contact their healthcare provider for evaluation if they experience swelling at or near the site of dermal filler following vaccination.

Vaccination of pregnant or lactating people

Pregnant people

Observational data demonstrate that while the absolute risk is low, pregnant people with COVID-19 have an increased risk of severe illness, including illness resulting in intensive care admission, mechanical ventilation, or death. Additionally, they might be at an increased risk of adverse pregnancy outcomes, such as preterm birth.

There are currently few data on the safety of COVID-19 vaccines, including mRNA vaccines, in pregnant people. Limited data are currently available from animal developmental and reproductive toxicity studies. No safety concerns were demonstrated in rats that received Moderna COVID-19 vaccine prior to or during gestation in terms of female reproduction, fetal/embryonal development, or postnatal development. Studies in pregnant people are planned and the vaccine manufacturers are following outcomes in people in the clinical trials who became pregnant. Based on current knowledge, experts believe that mRNA vaccines are unlikely to pose a risk to the pregnant person or the fetus because mRNA vaccines are not live vaccines. The mRNA in the vaccine is degraded quickly by normal cellular processes and does not enter the nucleus of the cell. However, the potential risks of mRNA vaccines to the pregnant person and the fetus are unknown because these vaccines have not been studied in pregnant people.

If pregnant people are part of a group that is recommended to receive a COVID-19 vaccine (e.g., healthcare personnel), they may choose to be vaccinated. A conversation between the patient and their clinical team may assist with decisions regarding the use of a mRNA COVID-19 vaccine, though a conversation with a healthcare provider is not required prior to vaccination. When making a decision, pregnant people and their healthcare providers should consider the level of COVID-19 community transmission, the patient's personal risk of contracting COVID-19, the risks of COVID-19 to the patient and potential risks to the fetus, the efficacy of the vaccine, the side effects of the vaccine, and the lack of data about the vaccine during pregnancy.

Side effects can occur with COVID-19 vaccine use in pregnant people, similar to those expected among non-pregnant people. Pregnant

people who experience fever following vaccination can be counseled to take acetaminophen because fever has been associated with adverse pregnancy outcomes. Acetaminophen can be offered as an option for pregnant people experiencing other post-vaccination symptoms.

There is no recommendation for routine pregnancy testing before receipt of a COVID-19 vaccine. Those who are trying to become pregnant do not need to avoid pregnancy after mRNA COVID-19 vaccination.

Lactating people

There are no data on the safety of COVID-19 vaccines in lactating people or the effects of mRNA COVID-19 vaccines on the breastfed infant or milk production/excretion. mRNA vaccines are not thought to be a risk to the breastfeeding infant. A lactating person who is part of a group recommended to receive a COVID-19 vaccine (e.g., healthcare personnel) may choose to be vaccinated.

Vaccination of children and adolescents

Adolescents aged 16–17 years are included among persons eligible to receive the Pfizer-BioNTech COVID-19 vaccine under the EUA. While vaccine safety and efficacy data in this age group are limited, there are no biologically plausible reasons for safety and efficacy profiles to be different than those observed in persons 18 years of age and older. Adolescents aged 16–17 years who are part of a group recommended to receive a COVID-19 vaccine may be vaccinated with the Pfizer-BioNTech COVID-19 vaccine with appropriate assent. Children and adolescents younger than 16 years of age are not authorized to receive the Pfizer-BioNTech COVID-19 vaccine at this time.

Children and adolescents younger than 18 years of age are not authorized to receive the Moderna COVID-19 vaccine at this time.

Patient counseling

Vaccine efficacy

Preliminary data suggest high vaccine efficacy in preventing COVID-19 following receipt of two doses of mRNA COVID-19 vaccine (Pfizer-BioNTech: 95.0% [95% CI: 90.3%, 97.6%]; Moderna: 94.1% [95% CI: 89.3%, 96.8%]). Limited data are currently available regarding the efficacy of a single dose. Patients should be counseled on the importance of completing the two-dose series with the same vaccine product to optimize protection.

Reactogenicity

Before vaccination, providers should counsel mRNA COVID-19 vaccine recipients about expected local (e.g., pain, swelling, erythema at the injection site, localized axillary lymphadenopathy on the same side as the vaccinated arm) and systemic (e.g., fever, fatigue, headache, chills, myalgia, arthralgia) post-vaccination symptoms. Depending on vaccine product (Pfizer vs. Moderna), age group, and vaccine dose, approximately 80–89% of vaccinated persons experience at least one local symptom and 55–83% experience at least one systemic symptom following vaccination.

Most systemic post-vaccination symptoms are mild to moderate in severity, occur within the first three days of vaccination, and resolve within 1–3 days of onset. These symptoms are more frequent and severe following the second dose and among younger persons

compared with older persons (i.e., ages >55 or ≥65 years [for Pfizer-BioNTech or Moderna vaccines, respectively]). Unless persons experience a contraindication to vaccination (see below), they should be encouraged to complete the series even if they experience local or systemic symptoms following the first dose to optimize protection against COVID-19.

In clinical trials, hypersensitivity-related adverse events were observed in 0.63% of participants who received the Pfizer-BioNTech COVID-19 vaccine and 1.5% of participants who received the Moderna COVID-19 vaccine, compared with 0.51% and 1.1%, respectively, in the placebo groups. Anaphylaxis following vaccination was not observed in the Pfizer-BioNTech or Moderna COVID-19 vaccines clinical trials. However, anaphylactic reactions have been reported following receipt of mRNA vaccines outside of clinical trials.

Management of post-vaccination symptoms

Antipyretic or analgesic medications (e.g., acetaminophen, non-steroidal anti-inflammatory drugs) can be taken for the treatment of post-vaccination local or systemic symptoms, if medically appropriate. However, routine prophylactic administration of these medications for the purpose of preventing post-vaccination symptoms is not currently recommended, because information on the impact of such use on mRNA COVID-19 vaccine-induced antibody responses is not available at this time.

In addition, administration of antihistamines to COVID-19 vaccine recipients prior to vaccination to prevent allergic reactions is not recommended. Antihistamines do not prevent anaphylaxis, and their use might mask cutaneous symptoms, which could lead to a delay in

the diagnosis and management of anaphylaxis. See section below ("contraindications and precautions to vaccination") and interim considerations for anaphylaxis management for more information on management of anaphylaxis.

Infection prevention and control considerations are available for healthcare personnel and long-term care facility residents (e.g., populations included in phase 1a of vaccine allocation) with systemic signs and symptoms following COVID-19 vaccination. Considerations may be updated as additional information becomes available or additional groups are prioritized for vaccine allocation.

Contraindications and precautions

While rare, anaphylactic reactions have been reported following vaccination with mRNA COVID-19 vaccines. Although investigations are ongoing, persons with a history of an immediate allergic reaction (of any severity) to an mRNA COVID-19 vaccine or any of its components might be at greater risk for anaphylaxis upon re-exposure to either of the currently authorized mRNA COVID-19 vaccines. For the purposes of this guidance, an immediate allergic reaction to a vaccine or medication is defined as any hypersensitivity-related signs or symptoms such as urticaria, angioedema, respiratory distress (e.g., wheezing, stridor), or anaphylaxis that occur within four hours following administration.

Recommendations for contraindications and precautions are described below and summarized in Appendix B. The following recommendations may change when further information becomes available.

Contraindications

CDC considers a history of the following to be a contraindication to vaccination with both the Pfizer-BioNTech and Moderna COVID-19 vaccines:

- Severe allergic reaction (e.g., anaphylaxis) after a previous dose of an mRNA COVID-19 vaccine or any of its components
- Immediate allergic reaction of any severity to a previous dose of an mRNA COVID-19 vaccine or any of its components (including polyethylene glycol [PEG])*
- Immediate allergic reaction of any severity to polysorbate (due to potential cross-reactive hypersensitivity with the vaccine ingredient PEG)*

* These persons should not receive mRNA COVID-19 vaccination (Pfizer-BioNTech or Moderna) at this time unless they have been evaluated by an allergist-immunologist and it is determined that the person can safely receive the vaccine (e.g., under observation, in a setting with advanced medical care available). See Appendix C for more information on ingredients included in mRNA COVID-19 vaccines.

Providers should attempt to determine whether reactions reported following vaccination are consistent with immediate allergic reactions versus other types of reactions commonly observed following vaccination, such as a vasovagal reaction or post-vaccination side effects (which are not contraindications to receiving the second vaccine dose) (Appendix D).

Healthcare personnel or health departments in the United States can request a consultation from the Clinical Immunization Safety Assessment COVIDvax project for a complex COVID-19 vaccine safety question about an individual patient residing in the United States not

readily addressed by CDC guidance.

Precautions

CDC considers a history of any immediate allergic reaction to any other vaccine or injectable therapy (i.e., intramuscular, intravenous, or subcutaneous vaccines or therapies [excluding subcutaneous immunotherapy for allergies , i.e. “allergy shots”] not related to a component of mRNA COVID-19 vaccines or polysorbate) as a precaution but not a contraindication to vaccination for both the Pfizer-BioNTech and Moderna COVID-19 vaccines. This includes persons with a reaction to a vaccine or injectable therapy that contains multiple components, one of which is PEG, another vaccine component, or polysorbate, but in whom it is unknown which component elicited the immediate allergic reaction.

Persons with a precaution to vaccination should be counseled about the unknown risks of experiencing a severe allergic reaction and balance these risks against the benefits of vaccination. Deferral of vaccination and/or consultation with an allergist-immunologist may be considered until further information on the risk of anaphylaxis is available. The following considerations can be used to help the provider conduct a risk assessment for mRNA COVID-19 vaccination in these individuals:

- Risk of exposure to SARS-CoV-2 (e.g., because of residence in a congregate setting such as a long-term care facility, occupation)
- Risk of severe disease or death due to COVID-19 (e.g., because of age, underlying medical conditions)
- Whether the patient has previously been infected with SARS-CoV-2 and, if so, how long ago

    - Note: Vaccination is recommended for persons with a history of COVID-19; however, because reinfection is uncommon in the months following infection, persons with a precaution to vaccination and recent COVID-19 may choose to defer vaccination until further information is known about the risk of anaphylaxis following vaccination.
- The unknown risk of anaphylaxis (including fatal anaphylaxis) following mRNA COVID-19 vaccination in a person with a history of an immediate allergic reaction to other vaccines or injectable therapies
- Ability of the patient to be vaccinated in a setting where appropriate medical care is immediately available for anaphylaxis

Neither contraindications nor precautions to vaccination

Allergic reactions (including severe allergic reactions) not related to vaccines, injectable therapies, components of mRNA COVID-19 vaccines (including PEG), or polysorbates, such as allergic reactions related to food, pet, venom, or environmental allergies, or allergies to oral medications (including the oral equivalents of injectable medications) are **not** a contraindication or precaution to vaccination with either mRNA COVID-19 vaccine. The vial stoppers of these mRNA vaccines are not made with natural rubber latex, and there is no contraindication or precaution to vaccination for persons with a latex allergy. In addition, because the mRNA COVID-19 vaccines do not contain eggs or gelatin, persons with allergies to these substances do not have a contraindication or precaution to vaccination.

Persons with only a delayed-onset local reaction (e.g., erythema, induration, pruritus) around the injection site area after the first vaccine dose do not have a contraindication or precaution to the second dose.

Delayed-onset local reactions have been reported in some individuals, including in Moderna clinical trial participants, beginning a few days through the second week after the first dose, and are sometimes quite large. It is not known whether persons who experienced a delayed-onset injection site reaction after the first dose will experience a similar reaction after the second dose. However, these delayed-onset local reactions are not felt to represent a risk for anaphylaxis upon receipt of the second dose. Thus, individuals with such delayed injection site reactions after the first mRNA COVID-19 vaccine dose should receive the second dose using the same vaccine product as the first dose and at the recommended interval, and preferably in the opposite arm.

Observation periods following vaccination (for persons without contraindications to mRNA COVID-19 vaccines)

CDC recommends an observation period following vaccination with mRNA COVID-19 vaccines. Persons with a history of an immediate allergic reaction of any severity to a vaccine or injectable therapy and persons with a history of anaphylaxis due to any cause should be observed for 30 minutes. All other persons should be observed for 15 minutes.

Management of anaphylaxis after mRNA COVID-19 vaccination

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of mRNA COVID-19 vaccine. Further information on anaphylaxis management can be found in the interim considerations for the management of anaphylaxis following COVID-19 vaccination and laboratory evaluation of persons who experience anaphylaxis after vaccination.

Public health recommendations for vaccinated persons

While mRNA COVID-19 vaccines have demonstrated high efficacy at preventing severe and symptomatic COVID-19, there is currently limited information on how much the vaccines might reduce transmission and how long protection lasts. In addition, the efficacy of the vaccines against emerging SARS-CoV-2 variants is not known. At this time, vaccinated persons should continue to follow **current guidance** to protect themselves and others, including wearing a mask, staying at least 6 feet away from others, avoiding crowds, avoiding poorly ventilated spaces, covering coughs and sneezes, washing hands often, following CDC travel guidance, and following any applicable workplace or school guidance, including guidance related to personal protective equipment use or SARS-CoV-2 testing.

However, vaccinated persons with an exposure to someone with suspected or confirmed COVID-19 are not required to quarantine if they meet all of the following criteria[†]:

- Are fully vaccinated (i.e., ≥2 weeks following receipt of the second dose in a 2-dose series, or ≥2 weeks following receipt of one dose of a single-dose vaccine)
- Are within 3 months following receipt of the last dose in the series
- Have remained asymptomatic since the current COVID-19 exposure

Persons who do not meet all 3 of the above criteria should continue to follow current quarantine guidance after exposure to someone with suspected or confirmed COVID-19.

Although the risk of SARS-CoV-2 transmission from vaccinated persons to others is still uncertain, vaccination has been demonstrated to prevent symptomatic COVID-19; symptomatic and pre-symptomatic transmission is thought to have a greater role in transmission than purely asymptomatic transmission. Additionally, individual and societal benefits of avoiding unnecessary quarantine may outweigh the potential but unknown risk of transmission, and facilitate the direction of public health resources to persons at highest risk for transmitting SARS-CoV-2 to others. This recommendation to waive quarantine for people with vaccine-derived immunity aligns with quarantine recommendations for those with natural immunity, which eases implementation.

Fully vaccinated persons who do not quarantine should still watch for symptoms of COVID-19 for 14 days following an exposure. If they experience symptoms, they should be clinically evaluated for COVID-19, including SARS-CoV-2 testing, if indicated. In addition, vaccinated persons should continue to follow **current guidance** to protect themselves and others, including all other SARS-CoV-2 testing recommendations and requirements, and state, territorial, tribal, and local travel recommendations or requirements. For additional considerations regarding quarantine or work restrictions for fully vaccinated healthcare personnel, patients, or residents in healthcare settings, please see section below.

These quarantine recommendations for vaccinated persons, including the criteria for timing since receipt of the last dose in the vaccination series, will be updated when more data become available and additional COVID-19 vaccines are authorized.

[†] CDC has not systematically evaluated the efficacy of COVID-19

vaccines from manufacturers that have not sought an EUA in the United States. For the purposes of these quarantine criteria, considerations for accepting a vaccination series that is not FDA-authorized include whether the vaccine product has received emergency approval from the World Health Organization or authorization from a national regulatory agency.

Vaccinated healthcare personnel, patients, and residents in healthcare settings

These criteria could also be applied when considering work restrictions for fully vaccinated healthcare personnel with higher-risk exposures, as a strategy to alleviate staffing shortages. Of note, exposed healthcare personnel would not be required to quarantine outside of work.

As an exception to the above guidance no longer requiring quarantine for fully vaccinated persons, **vaccinated inpatients and residents in healthcare settings should continue to quarantine following an exposure** to someone with suspected or confirmed COVID-19; outpatients should be cared for using appropriate Transmission-Based Precautions. This exception is due to the unknown vaccine effectiveness in this population, the higher risk of severe disease and death, and challenges with social distancing in healthcare settings. Although not preferred, healthcare facilities could consider waiving quarantine for vaccinated patients and residents as a strategy to mitigate critical issues (e.g., lack of space, staff, or PPE to safely care for exposed patients or residents) when other options are unsuccessful or unavailable. These decisions could be made in consultation with public health officials and infection control experts.

CDC's healthcare infection control guidance contains additional

considerations regarding the need to protect healthcare personnel, patients, and residents while also alleviating any staffing shortages.

Reporting of vaccine adverse events

Adverse events that occur in a recipient following mRNA COVID-19 vaccination should be reported to VAERS. Vaccination providers are required by the Food and Drug Administration to report the following that occur after mRNA COVID-19 vaccination under Emergency Use Authorization:

- 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 any other clinically significant adverse event even if it is uncertain whether the vaccine caused the event. Information on how to submit a report to VAERS is available at https://vaers.hhs.gov or by calling 1-800-822-7967.

In addition, CDC has developed a new, voluntary smartphone-based tool, v-safe. This tool uses text messaging and web surveys to provide near real-time health check-ins after patients receive COVID-19 vaccination. Reports to v-safe indicating a medically significant health impact, including pregnancy, are followed up by the CDC/v-safe call center to collect additional information to complete a VAERS report, if appropriate.

Laboratory testing

Interpretation of SARS-CoV-2 test results in vaccinated persons

Prior receipt of an mRNA COVID-19 vaccine will not affect the results of SARS-CoV-2 viral tests (nucleic acid amplification or antigen tests). Currently available antibody tests for SARS-CoV-2 assess IgM and/or IgG to one of two viral proteins: spike or nucleocapsid. Because both the Pfizer-BioNTech and Moderna COVID-19 vaccines contain mRNA that encodes the spike protein, a positive test for spike protein IgM/IgG could indicate either prior infection or vaccination. To evaluate for evidence of prior infection in an individual with a history of mRNA COVID-19 vaccination, a test specifically evaluating IgM/IgG to the nucleocapsid protein should be used. Antibody testing is not currently recommended to assess for immunity to COVID-19 following mRNA COVID-19 vaccination or to assess the need for vaccination in an unvaccinated person.

Use of immune-based tests for tuberculosis infection, such as the tuberculin skin test and interferon-gamma release assay

The mRNA COVID-19 vaccine should not be delayed because of testing for TB infection. Testing for TB infection with one of the immune-based methods, either the tuberculin skin test (TST) or an interferon release assay (IGRA), can be done before or during the same encounter as the mRNA COVID-19 vaccination. When testing with TST or IGRA cannot be done at the same time as mRNA COVID-19 vaccination, these tests should be delayed ≥4 weeks after the completion of mRNA COVID-19 vaccination but generally should not be cancelled.

Patients who have active TB disease or an illness that is being evaluated as active TB disease can receive an mRNA COVID-19

vaccine (note: the presence of a moderate or severe acute illness is a precaution to administration of all vaccines). Whereas a TST or IGRA test is part of a comprehensive evaluation for TB disease, positive TST or IGRA results are not required to diagnose active TB disease.

When considering a tuberculin skin test or interferon-gamma release assay:

- The TST is not expected to have an effect on the safety or the effectiveness of the mRNA COVID-19 vaccine. IGRAs are blood tests and thus do not affect vaccine safety or effectiveness.
- The reliability of a positive TST or IGRA result after mRNA COVID-19 vaccination is expected to be the same as without the vaccination. mRNA COVID-19 vaccination is not expected to cause false positive results from a TB test that is done at the same encounter as or after mRNA COVID-19 vaccination.
- The reliability of a negative TST or IGRA result after mRNA COVID-19 vaccination has not been studied.
- The TST is not a vaccine. The guidance for separating other vaccines from mRNA COVID-19 vaccination by at least 2 weeks in time does not apply to the TST because the TST is not a vaccine.

When a tuberculin skin test or interferon gamma release assay is required by policy:

- A TST or IGRA to meet administrative requirements, (for example, for healthcare employment or for admission to long-term care), can be done prior to mRNA COVID-19 vaccination or at the same encounter. The mRNA COVID-19 vaccine should not be delayed because of testing for TB infection.
- A TST or IGRA should be deferred until ≥4 weeks after the

completion of mRNA COVID-19 vaccination. If testing requirements or policies cannot be modified for the COVID-19 pandemic to accept this delay in TST or IGRA testing, it should be understood that a false negative TST or IGRA cannot be excluded, and consideration should be given to repeating negative TST or IGRA tests at least 4 weeks after the completion of COVID-19 mRNA vaccination. If TST was the initial test, boosting could be a factor if the result of the repeat test is positive.

When a tuberculin skin test or interferon gamma release assay is indicated for medical care:

- The decision as to whether a TST or IGRA that is being done for medical diagnosis of latent TB infection, (for example, during a contact investigation after exposure to contagious TB disease) should be delayed for 4 weeks after completion of COVID-19 mRNA vaccination is at the discretion of the responsible medical provider and local tuberculosis program overseeing the contact investigation. Medical providers and local tuberculosis programs may not wish to delay testing for persons at high risk for progression to TB disease. However, patients who have a negative result in this context should be considered for retesting ≥4 weeks after the completion of mRNA COVID-19 vaccination.
- Patients who have symptoms or diagnostic findings consistent with active TB disease should receive further medical evaluation, for example, with chest radiography and sputum bacteriology for *Mycobacterium tuberculosis*, regardless of TST or IGRA results.

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.
	• Second dose administered more than 42 days after the first dose	• Do **not** repeat dose. This deviation from CDC guidance does **not** require VAERS reporting.
	• Dose administered within 14 days before or after another (i.e., non-COVID-19) vaccine	• Do **not** repeat COVID-19 vaccine* or other vaccine(s) doses. This deviation from CDC guidance does **not** require VAERS reporting.
Mixed series	• Incorrect mRNA COVID-19 vaccine product administered for second dose in 2-dose series	• Do **not** repeat dose. §
	• Higher-than-authorized dose volume administered	• Do **not** repeat dose. *† Inform the recipient of the potential for local and systemic adverse events.
	• Lower-than-	• If more than half of the dose was administered, do **not**

Dosage	authorized dose volume administered (e.g., leaked out, equipment failure, recipient pulled away)	repeat dose.* • If less than half of the dose was administered or the proportion of the dose cannot be estimated, administer the authorized dose immediately (no minimum interval) in the opposite arm.#
Storage and handling	• Dose administered after improper storage and handling (e.g., temperature excursion, more than 6 hours after first vial puncture)	• Contact the manufacturer for guidance. If the manufacturer provides information supporting that the dose should be repeated, the repeated dose may be given immediately (no minimum interval) in the opposite arm.
	• Dose administered past the expiration/beyond use date	• Contact the manufacturer for guidance. If the manufacturer provides information supporting that the dose should be repeated, the repeated dose may be given immediately (no minimum interval) in the opposite arm.
	• ONLY diluent administered (i.e., sterile 0.9% sodium chloride)	• Inform the recipient that no vaccine was administered. Administer the authorized dose immediately (no minimum interval) in the opposite arm.#
	• No diluent, resulting in higher than authorized	• Do **not** repeat dose*† Inform the recipient of the potential

	dose (i.e., 0.3 ml of undiluted vaccine administered)	for local and systemic adverse events.
Diluent (Pfizer-BioNTech only)	• Incorrect diluent type (e.g., sterile water, bacteriostatic 0.9% NS)	• Contact the manufacturer for guidance. If the manufacturer provides information supporting that the dose should be repeated, the repeated dose may be given immediately (no minimum interval) in the opposite arm.
	• Incorrect diluent volume (i.e., the vial contents were diluted with a diluent volume other than 1.8 ml, but a 0.3 ml dose was still administered)	• For doses administered with diluent volume less than 1.8 ml, Inform the recipient of the potential for local and systemic adverse events. * † • For doses administered with diluent volume greater than 1.8 ml, do **not** repeat dose. * (Note: dilution with a volume up to 4.0 ml [which exceeds vial capacity] results in more-than-half of the authorized dose administered).

* If the dose given in error is the first dose, a second dose should be administered at the recommended interval (21 days [Pfizer-BioNTech] or 28 days [Moderna]). If this dose is the second dose, the series is complete and no additional doses are needed.

If the dose given in error is the first dose, the second dose should be administered at the recommended interval (21 days [Pfizer-BioNTech] or 28 days [Moderna]) from the date of receipt of the valid dose (not

the date of receipt of the erroneous dose).

[∞] Do not administer the second dose until the person becomes eligible to receive vaccination (either by reaching the authorized age or if the authorization is extended to include additional age groups), even if this results in the second dose being administered after the recommended interval between doses.

[†] If the administration error resulted in a higher-than-authorized vaccine dose, in general the second dose may still be administered at the recommended interval. However, if local or systemic side effects following vaccination are clinically concerning (outside of the expected side effect profile), lead to serious adverse reactions, or are ongoing at the time of the second dose, the decision to administer the second dose may be assessed on a case-by-case basis.

[§] Although CDC provides considerations for a mixed series in exceptional circumstances, this is still considered an administration error that requires VAERS reporting (as a mixed series is not authorized under the vaccine Emergency Use Authorizations).

Appendix B: Triage of persons presenting for mRNA COVID-19 vaccination

[*] PEG and polysorbate are common excipients in many vaccines, injectable therapies, and other products. Persons with a known (diagnosed) allergy to PEG, another mRNA vaccine component, or polysorbate, have a contraindication to vaccination. Persons with a reaction to a vaccine or injectable therapy that contains multiple components, one of which is PEG, another mRNA vaccine component or polysorbate, but in whom it is unknown which component elicited

the immediate allergic reaction have a precaution to 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.

^ See Appendix B for a list of ingredients. Note: Polyethylene glycol (PEG), an ingredient in both mRNA COVID-19 vaccines, is structurally related to polysorbate and cross-reactive hypersensitivity between these compounds may occur. Information on ingredients of a vaccine or medication (including PEG, a PEG derivative, or polysorbates) can be found in the package insert.

These persons should not receive mRNA COVID-19 vaccination at this time unless they have been evaluated by an allergist-immunologist and it is determined that the person can safely receive the vaccine (e.g., under observation, in a setting with advanced medical care available)

Appendix C: Ingredients included in Pfizer-BioNTech and Moderna mRNA COVID-19 vaccines

An immediate allergic reaction to any component or previous dose of an mRNA COVID-19 vaccine is a contraindication to vaccination with both the Pfizer-BioNTech and Moderna vaccines. The following is a list of ingredients for the Pfizer-BioNTech and Moderna COVID-19 vaccines reported in the prescribing information for each vaccine.

* Neither vaccine contain eggs, gelatin, latex, or preservatives

Note: Both the Pfizer-BioNTech and Moderna COVID-19 vaccines

contain polyethylene glycol (PEG). PEG is a primary ingredient in osmotic laxatives and oral bowel preparations for colonoscopy procedures, an inactive ingredient or excipient in many medications, and is used in a process called pegylation to improve the therapeutic activity of some medications (including certain chemotherapeutics). Additionally, cross-reactive hypersensitivity between PEG and polysorbates (included as an excipient in some vaccines and other therapeutic agents) can occur.

Information on whether a medication contains PEG, a PEG derivative, or polysorbates as either active or inactive ingredients can be found in the package insert. The National Institutes of Health DailyMed database can also be used as a resource. As of January 21, 2021, mRNA COVID-19 vaccines are the only currently available vaccines in the United States that contain PEG, though several vaccines contain polysorbate (more information can be found in CDC's vaccine excipient summary). Some medications that contain PEG and/or polysorbate are also described in the supplementary materials of Stone CA, et al. "Immediate hypersensitivity to polyethylene glycols and polysorbates: more common than we have recognized." *The Journal of Allergy and Clinical Immunology: In Practice* 7.5 (2019): 1533-1540. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6706272/pdf/nihms-1019221.pdf

Appendix D: Potential characteristics of allergic reactions, vasovagal reactions, and vaccine side effects following mRNA COVID-19 vaccination

In patients who experience post-vaccination symptoms, determining the etiology (including allergic reaction, vasovagal reaction, or vaccine

side effects) is important to determine whether a person can receive additional doses of mRNA COVID-19 vaccines. The following table of signs and symptoms is meant to serve as a resource but might not be exhaustive, and patients might not have all signs or symptoms. Providers should use their clinical judgement when assessing patients to determine the diagnosis and management.

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