Emergency Use Instructions for Healthcare Providers:
Moderna COVID-19 vaccine for Primary, Additional, and/or Booster Doses

The Centers for Disease Control and Prevention (CDC) is issuing Emergency Use Instructions (EUI) to provide information about the use of the COVID-19 vaccine by Moderna (Spikevax), which is approved (licensed) by the Food and Drug Administration (FDA) for the prevention of COVID-19 in individuals 18 years and older.[1] The CDC-issued EUI provide instructions and information for the use of this vaccine that are beyond the FDA-approved labeling. The CDC-issued EUI provide information on the following uses of the COVID-19 vaccine by Moderna for:

- primary dose(s) in those with certain immunocompromising conditions or those with incomplete primary dose series, and/or a booster dose for persons 18 years and older who received primary vaccination with certain **non-FDA authorized or approved** COVID-19 vaccines[2].
- a 3-month interval for the booster dose after an mRNA vaccine primary series for persons 18 years and older who are moderately or severely immunocompromised.
- an additional dose in persons 18 years and older with certain immunocompromising conditions who received primary vaccination with the Janssen COVID-19 Vaccine.
- revaccination of moderately or severely immunocompromised persons 18 years and older who received certain therapies (i.e., hematopoietic cell transplant (HCT) or chimeric antigen receptor (CAR)-T-cell therapy) and received dose(s) of COVID-19 vaccine prior to or during treatment.

mRNA vaccines are preferred for persons with moderate or severe immune compromise. The COVID-19 vaccine by Pfizer-BioNTech under EUI also allow similar uses in persons 12 years and older as an alternative mRNA COVID-19 vaccine to Moderna, and the same or similar recommendations in the EUI also apply to the use of the COVID-19 vaccine by Pfizer-BioNTech under EUI. See the Pfizer-BioNTech COVID-19 EUI Fact Sheet for Healthcare Providers.

Refer to CDC's Interim Clinical Considerations for specific recommendations on use of the COVID-19 vaccine by Moderna allowed under the EUI. Relevant information is detailed in the sections titled: "People who received COVID-19 vaccine outside the United States", "People who received COVID-19 vaccine as part of a clinical trial", and "Recommendations for COVID-19 vaccination in moderately or severely immunocompromised people." For additional information about the COVID-19 vaccine by Moderna COVID-19, refer to the Spikevax package insert or the Full EUA Prescribing Information (FDA, 2022).

What are EUI and why is CDC issuing EUI for the COVID-19 vaccine by Moderna?
In 2013, the Pandemic and All-Hazards Preparedness Reauthorization Act included a new provision that allowed for the issuance of EUI to permit CDC to inform healthcare providers and recipients about certain uses of FDA-approved or cleared medical products. Specifically, EUI inform healthcare providers and recipients about such products' approved, licensed, or cleared conditions of use. The CDC Director has statutory (legal) authority to create, issue, and disseminate EUI before or during an emergency.

The COVID-19 vaccine by Moderna was approved by the FDA on January 31, 2022 as a 2-dose primary series for active immunization to prevent COVID-19 in persons 18 years and older. CDC is issuing these EUI to provide information about use of the COVID-19 vaccine by Moderna for persons 18 years and older as primary dose(s) in those with certain immunocompromising conditions or those with incomplete primary dose series, and/or a

[1] Spikevax is the proprietary name for the product licensed under the Biologics License Application (BLA). The Moderna COVID-19 Vaccine has been available since December 18, 2020, pursuant to Emergency Use Authorization (EUA). The approved formulation of Spikevax and the FDA-authorized Moderna COVID-19 Vaccine for ≥ 18 years are the same formulation. Because of these features, and because Spikevax may be commonly referred to as the "Moderna COVID-19 Vaccine," these EUI refer to this vaccine as the COVID-19 vaccine by Moderna.

[2] A non-FDA authorized or approved COVID-19 vaccine that is listed for emergency use by the World Health Organization, or is included in CDC's Technical Instructions for Implementing Presidential Proclamation Advancing Safe Resumption of Global Travel During the COVID-19 Pandemic and CDC's Order, or that is a non-placebo part of a clinical trial within or outside the United States that is a WHO-EUL COVID-19 vaccine or a vaccine that is not listed for emergency use by WHO but for which a U.S. data and safety monitoring board or equivalent has independently confirmed efficacy in the United States (hereinafter "non-FDA authorized or approved COVID-19 vaccines").

booster dose in those who received primary vaccination with certain **non-FDA authorized or approved** COVID-19 vaccines. For example, these EUI cover use of the COVID-19 vaccine by Moderna in individuals who were vaccinated outside of the United States or in clinical trials with the AstraZeneca COVID-19 vaccine, the Novavax COVID-19 vaccine, or the Sinopharm COVID-19 vaccine, among others. The EUI also provide for heterologous use of the COVID-19 vaccine by Moderna as an additional dose in persons 18 years and older with certain immunocompromising conditions who completed primary vaccination with the FDA-authorized Janssen COVID-19 Vaccine. Additionally, the EUI provide for revaccination of moderately or severely immunocompromised persons 18 years and older who received certain therapies (i.e. HCT or CAR-T-cell therapy) and received dose(s) of COVID-19 vaccine prior to or during treatment.

What is COVID-19?

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-CoV-2, that emerged in late 2019. It is predominantly a respiratory illness that can affect other organs. People with SARS-CoV-2 infection have reported a wide range of symptoms, ranging from no symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include fever or chills, cough, shortness of breath, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, and diarrhea.

Who can receive the COVID-19 vaccine by Moderna?

The below describes who can receive the COVID-19 vaccine by Moderna under EUI. The COVID-19 vaccine by Pfizer-BioNTech can also be used under EUI for similar uses in those 12 years and older as an alternative mRNA COVID-19 vaccine (see the Pfizer-BioNTech EUI Fact Sheet for Healthcare Providers).

- Certain moderately and severely immunocompromised persons 18 years and older who received primary vaccination with certain non-FDA authorized or approved COVID-19 vaccines should receive an additional primary dose of the COVID-19 vaccine by Moderna.
- Persons 18 years and older who received incomplete primary dose series (e.g., only the first dose of 2-dose primary series) with certain non-FDA authorized or approved COVID-19 vaccines should receive a primary dose of the COVID-19 vaccine by Moderna.
- Persons 18 years and older who have received primary vaccination with certain non-FDA authorized or approved COVID-19 vaccines should receive a booster dose of the COVID-19 vaccine by Moderna.
- Certain moderately and severely immunocompromised persons 18 years and older who received primary vaccination with the Janssen COVID-19 Vaccine should receive an additional dose with the COVID-19 vaccine by Moderna.
- Moderately or severely immunocompromised persons 18 years and older who received certain therapies (i.e., HCT or CAR-T-cell therapy) and received dose(s) of COVID-19 vaccine prior to or during treatment should be revaccinated with the COVID-19 vaccine by Moderna for any doses received before or during treatment.

What are the doses and intervals of the COVID-19 vaccine by Moderna for primary, additional, and/or booster doses?

- A primary dose, including as an additional primary dose for those with certain immunocompromising conditions, of the COVID-19 vaccine by Moderna (100 µg in 0.5 mL) should be administered intramuscularly at least 28 days after primary vaccination with certain non-FDA authorized or approved COVID-19 vaccines.
- A booster dose of the COVID-19 vaccine by Moderna (50 µg in 0.25 mL) should be administered intramuscularly for persons who completed primary vaccination with a series that included certain non-FDA authorized or approved COVID-19 vaccines: at least 3 months after completion of primary vaccination for immunocompromised persons or at least 5 months after completion of primary vaccination for non-immunocompromised persons.
- An additional dose with the COVID-19 vaccine by Moderna (100 µg in 0.5 mL) should be administered intramuscularly for persons with certain immunocompromising conditions at least 28 days after completion of primary vaccination with the Janssen COVID-19 Vaccine (e.g., 1 primary dose of the Janssen COVID-19 Vaccine followed by an additional dose with Moderna vaccine at least 28 days after the primary dose). People who received 1 primary dose of the Janssen COVID-19 Vaccine and 1 booster of an authorized COVID-19 vaccine, should receive an additional dose with the COVID-19 vaccine by Moderna at least 2 months after the booster dose.
- Revaccination with the COVID-19 vaccine by Pfizer-BioNTech at least 3 months after therapy for any doses received before or during treatment with certain therapies (i.e., HCT or CAR-T-cell therapy).

See Table 3 COVID-19 vaccination schedule for moderately or severely immunocompromised people in CDC's Interim Clinical Considerations for the latest dosing recommendations.

On a case-by-case basis, providers of moderately or severely immunocompromised patients may administer the COVID-19 vaccine by Moderna outside of the FDA-authorized or FDA-approved labeling and CDC recommended dosing intervals based on clinical judgment when the benefits of vaccination are deemed to outweigh the potential and unknown risks for the recipient.

Refer to CDC's Interim Clinical Considerations for specific and the latest dosing recommendations (e.g., number of doses, dosing intervals, revaccination) that may vary for individuals with certain medical conditions and/or in certain circumstances, which differ from or extend beyond the FDA-authorized and/or FDA-approved labeling.

What are the formulations of the COVID-19 vaccine by Moderna that these EUI apply to?

The EUI apply to the FDA-approved formulation of the COVID-19 vaccine by Moderna. As of January 31, 2022, there is one FDA-approved formulation of this vaccine, which has a red vial cap. The formulation is also FDA-authorized under EUA and provides 0.5 mL primary doses (containing 100 µg mRNA) and 0.25 ml booster doses (containing 50 µg mRNA). FDA has explained that FDA-approved Spikevax and the EUA-authorized Moderna COVID-19 vaccine have the same formulation and can be used interchangeably without presenting any safety or effectiveness concerns.

What are the common side effects with the COVID-19 vaccine by Moderna?

Adverse reactions following administration of the vaccine that have been reported in clinical trials and/or post authorization include injection site pain, fatigue, headache, muscle pain, joint pain, chills, nausea, vomiting, axillary swelling/tenderness, fever, injection site swelling, injection site redness, and rash.

What are possible serious side effects with the COVID-19 vaccine by Moderna?

Anaphylaxis and other severe allergic reactions, myocarditis, pericarditis, and syncope have been reported following administration of the vaccine outside of clinical trials. The observed risk of myocarditis and pericarditis is highest in males 18 through 24 years of age. Some observational analyses of postmarketing data suggest that there may be an increased risk of myocarditis and pericarditis in males under 40 years of age

following the second dose of the COVID-19 vaccine by Moderna relative to other authorized or approved mRNA COVID-19 vaccines. Although postmarketing data following a booster dose of mRNA vaccines are limited, available evidence suggests a lower myocarditis risk following a booster dose relative to the risk following the primary series second dose.

Who should not receive the COVID-19 vaccine by Moderna?
Do not administer the COVID-19 vaccine by Moderna to persons with known history of a severe allergic reaction (e.g., anaphylaxis) to a previous dose or any component of the vaccine (see *Contraindications, and Warnings and Precautions* sections in the Spikevax package insert or Full EUA Prescribing Information as well as CDC's Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Approved or Authorized in the United States for additional considerations).

What information should be provided to persons receiving a primary, additional, and/or booster dose of the COVID-19 vaccine by Moderna as described in the EUI?

- Provide the EUI Fact Sheet for Recipients and Caregivers.
- Provide a CDC COVID-19 Vaccination Record Card to the recipient or their caregiver with the lot number and date of administration recorded for the primary, additional, or booster dose of the COVID-19 vaccine by Moderna.
- Provide the v-safe information sheet to vaccine recipients/caregivers and encourage vaccine recipients to participate in v-safe. V-safe is a voluntary smartphone-based tool that uses text messaging and web surveys to check in with people who have been vaccinated to identify potential side effects after COVID-19 vaccination. V-safe asks questions that help CDC monitor the safety of COVID-19 vaccines. For more information, visit: www.cdc.gov/vsafe.

What is the available supporting evidence for use of the COVID-19 vaccine by Moderna for additional primary or booster doses in people who received a primary vaccination with non-FDA authorized or approved COVID-19 vaccines?
CDC has not systematically evaluated the safety, immunogenicity, and efficacy of an additional dose of the COVID-19 vaccine by Moderna (as either an additional primary dose for immunocompromised or as a booster dose) following receipt of primary vaccination with a non-FDA authorized or approved COVID-19 vaccine. However, studies of COVID-19 vaccine boosting in the United Kingdom have shown that a third dose of AstraZeneca, Moderna, or Pfizer-BioNTech COVID-19 vaccines successfully boosted immune responses in people who had been primed with two doses of Pfizer-BioNTech or AstraZeneca COVID-19 vaccines approximately 3 months earlier. Levels of binding (IgG) and neutralizing antibodies, including against Delta variant, were generally higher when an mRNA vaccine was used as either a heterologous or homologous boost (Munro et al., 2021)). Frequencies of local and systemic adverse reactions in the 7 days post booster vaccination were higher with heterologous than homologous boosters and in those aged under 70 years when compared to older recipients. Among all mRNA vaccines, the 100 microgram COVID-19 vaccine by Moderna was the most reactogenic (Munro et al., 2021).

WHO's Strategic Advisory Group of Experts (SAGE) on Immunization has noted that although data are currently limited on the safety, immunogenicity, and effectiveness of heterologous versus homologous additional doses, evolving evidence suggests that use of a heterologous vaccine for an additional dose may be more immunogenic than a homologous series. In its recommendations for an additional dose in certain immunocompromised people and in people aged 60 years and over who received Sinopharm BIBP or Sinovac-CoronaVac COVID-19 vaccines as a 2-dose primary series, WHO has advised that countries can consider heterologous additional doses based on supply availability (WHO SAGE, 2021a-c).

More than 80 countries are using boosters after non-FDA authorized or approved COVID-19 vaccines. Countries such as the United Kingdom (JCVI, 2021a-b), Canada (National Advisory Committee on Vaccination, 2021), Germany, and France have recommended heterologous dosing, including with use of the Moderna COVID-19 vaccine, for an additional primary series and/or booster dose based on their reviews of available immunological and safety data, as well as the epidemiology of COVID-19 and other contextual factors.

Effectiveness of a Moderna COVID-19 Vaccine (0.25 mL [50 µg of mRNA]) booster dose in individuals who completed primary vaccination with another authorized or approved COVID-19 Vaccine (homologous or heterologous booster dose) is inferred from immunogenicity data supporting effectiveness of a Moderna COVID-19 Vaccine (0.25 mL) booster dose administered following completion of a Moderna COVID-19 Vaccine primary series and from immunogenicity data from an independent Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States that evaluated a booster dose (0.5 mL) of the Moderna COVID-19 Vaccine. In this study, adults who had completed primary vaccination with a Moderna COVID-19 Vaccine 2-dose series (N=151), a Janssen COVID-19 Vaccine single dose (N=156), or a Pfizer-BioNTech COVID-19 Vaccine 2-dose series (N=151) at least 12 weeks (range 12 to 20 weeks) prior to enrollment and who reported no history of SARS-CoV-2 infection were randomized 1:1:1 to receive a booster dose of one of three vaccines: Moderna COVID-19 Vaccine, Janssen COVID-19 Vaccine, or Pfizer-BioNTech COVID-19 Vaccine. Neutralizing antibody titers, as measured by a pseudovirus neutralization assay using a lentivirus expressing the SARS-CoV-2 Spike protein with D614G mutation, were assessed on Day 1 prior to administration of the booster dose and on Day 15 after the booster dose. A booster response to the Moderna COVID-19 Vaccine (0.5 mL) was demonstrated regardless of primary vaccination.

Recent studies indicate that additional doses in people who are moderately or severely immunocompromised are safe and can increase antibody response. Small studies in solid organ transplant recipients in Toulouse, Strasbourg, and Baltimore demonstrate immunogenicity of a 4th mRNA dose when administered 1–2 months after the 3rd dose (Kamar et al., 2021; Benotmane et al., preprint; Alejo et al., 2021). Multiple studies, including COV-BOOST and the NIH mix-and-match study demonstrated safety and immunogenicity of a booster dose in the general population when administered at intervals as short as 3 months following a 2-dose primary series (Munro et al., 2021; Atmar et al., preprint). Finally, multiple countries have implemented booster doses at least 3 months after primary vaccination in the general population (e.g., UK, Germany, Netherlands).

Risk-Benefit of the COVID-19 vaccine by Moderna Additional Primary or Booster Vaccination for Individuals Described in the EUI

The duration of vaccine-induced protection from primary vaccination with COVID-19 vaccines is unknown. Efficacy data from clinical studies of 2-dose primary series supported benefit of the COVID-19 vaccine by Moderna in preventing severe COVID-19 and supported its FDA approval. Effectiveness of an additional primary dose of the COVID-19 vaccine by Moderna is inferred from immunogenicity data in immunocompromised adults who received a third 0.5 mL primary dose. Rates of local or systemic adverse events with 50 µg booster dose were comparable to those observed after Dose 2 of the primary series (Miller, 2021; Das, 2021).

Effectiveness of a heterologous booster dose of COVID-19 vaccine by Moderna is inferred from data in adults who received a booster dose following primary vaccination with the Moderna COVID-19 vaccine or another FDA-authorized COVID-19 vaccine. Available data on the safety or efficacy of a Moderna COVID-19 vaccine dose after receipt of a non-FDA authorized or approved COVID-19 vaccine are limited. However, based on available information, it appears reasonable to anticipate that known and potential risks of an additional primary dose or a booster dose of the COVID-19 vaccine by Moderna may be outweighed by its likely benefit to enhance or restore protection by the primary vaccination, which might have waned over time, especially in people with immunocompromising conditions or taking immunosuppressive medications who may require a shorter interval for booster doses.

Refer to the CDC's Interim Clinical Considerations for Use of COVID-19 Vaccines for additional information.

Available Alternatives
Currently, the Moderna COVID-19 vaccine and Pfizer-BioNTech COVID-19 vaccine are the only FDA-approved vaccines for which EUI provide for primary, additional, and/or booster dose administration.

Reporting Adverse Event or Medication Errors
The vaccination provider is responsible for mandatory reporting of the following to the Vaccine Adverse Event Reporting System (VAERS):

- vaccine administration errors whether or not associated with an adverse event,
- serious adverse events (irrespective of attribution to vaccination),
- cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and
- cases of COVID-19 that result in hospitalization or death.

Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html.
For further assistance with reporting to VAERS call 1-800-822-7967.

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