PLEASE READ THIS COVID-19 VACCINE NOTICE CAREFULLY BEFORE PURCHASING ANY COVID-19 VACCINES (DEFINED BELOW). THE COVID-19 VACCINES HAVE BEEN AUTHORIZED BY THE FDA UNDER AN EMERGENCY USE AUTHORIZATION (THE "EUA"). THE EUA AND THIS NOTICE CONTAIN VERY IMPORTANT INFORMATION ABOUT CUSTOMER'S OBLIGATIONS, INCLUDING WITH RESPECT TO THE CLINICAL ADMINISTRATION OF THE COVID-19 VACCINES.

Information Relating to the COVID-19 Vaccines and Conditions of Use

a. The Moderna COVID-19 Vaccine (2024-2025 Formula) (the "COVID-19 Vaccine") has not been approved or licensed by FDA, but has been authorized for emergency use by the FDA, under an Emergency Use Authorization ("EUA") to prevent Coronavirus Disease 2019 (COVID-19) for use in individuals aged 6 months through 11 years of age. The emergency use of this COVID-19 Vaccine is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of the medical product under Section 564(b)(1) of the FD&C Act unless the declaration is terminated or authorization revoked sooner.

b. There are requirements in the EUA that apply to Vaccination Providers.[1] Please review the EUA carefully to ensure that you understand and comply with the requirements that apply to you. See EUA (Exhibit A).

c. Please also review and distribute as required: (1) the Fact Sheet for Healthcare Providers Administering Vaccine: Emergency Use Authorization of Moderna COVID-19 Vaccine (2024-2025 Formula) For Individuals 6 Months Through 11 Years of Age (Exhibit B), and (2) Fact Sheet for Recipients and Caregivers About Moderna COVID-19 Vaccine (2024-2025 Formula) Which Has Emergency Use Authorization (EUA) to Prevent Coronavirus Disease 2019 (COVID-19) in Individuals 6 Months Through 11 Years of Age (Exhibit C).

[1]"Vaccination Provider" refers to the facility, organization, or healthcare provider (e.g., non-physician healthcare professionals, such as nurses, pharmacists) licensed or otherwise authorized to administer or provide vaccination services pursuant to State law. If the vaccine is exported from the United States, a "vaccination provider" is a provider that is authorized to administer this vaccine in accordance with the laws of the country in which it is administered. For purposes of this letter, "vaccination provider" also includes a person authorized by the U.S. Department of Health and Human Services (e.g., under the PREP Act Declaration for Medical Countermeasures against COVID-19) to administer FDA-authorized COVID-19 vaccine (e.g., qualified pharmacy technicians and State-authorized pharmacy interns acting under the supervision of a qualified pharmacist). See, e.g., HHS, E*leventh Amendment to the Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19 and Republication of the Declaration*. (88 FR 30769, May 12, 2023). In addition, for purposes of this letter, the term "State" includes any State or Territory of the United States, the District of Columbia, and the Commonwealth of Puerto Rico. See Section 201(a)(1) of the Act.

EXHIBIT A

Emergency Use Authorization

(Starts on Following Page)

August 22, 2024

ModernaTX, Inc.
Attention: Ms. Biliana Nestorova
200 Technology Square
Cambridge, MA 02139

Dear Ms. Nestorova :

On February 4, 2020, as amended on March 15, 2023, pursuant to Section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act or the Act), the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency, or a significant potential for a public health emergency, that affects, or has a significant potential to affect, national security or the health and security of United States citizens living abroad, and that involves the virus that causes Coronavirus Disease 2019 (COVID-19).[1] On the basis of such determination, the Secretary of HHS on March 27, 2020, declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to Section 564 of the Act (21 U.S.C. 360bbb-3), subject to the terms of any authorization issued under that section.[2]

On December 18, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for emergency use of Moderna COVID-19 Vaccine (Original monovalent)[3] for the prevention of COVID-19 for individuals 18 years of age and older, pursuant to Section 564 of the Act.

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[1] U.S. Department of Health and Human Services, Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3. February 4, 2020. U.S. Department of Health and Human Services, *Amended Determination of a Public Health Emergency or Significant Potential for a Public Health Emergency Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)*. March 15, 2023. 88 FR 16644 (March 20, 2023) ("Amended Determination").

[2] U.S. Department of Health and Human Services, Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3, 85 FR 18250 (April 1, 2020). See Amended Determination ("The declarations issued pursuant to section 564(b)(1) of the FD&C Act that circumstances exist justifying the authorization of emergency use of certain in vitro diagnostics, personal respiratory protective devices, other medical devices and drugs and biological products, as set forth in those declarations, and that are based on the February 4, 2020 determination, remain in effect until those declarations are terminated in accordance with section 564 of the FD&C Act.").

[3] For purposes of this letter, Moderna COVID-19 Vaccine (Original monovalent) refers to the vaccine that encodes the spike protein of only the Original SARS-CoV-2.

FDA reissued the letter of authorization on: February 25, 2021,[4] July 7, 2021,[5] August 12, 2021,[6] October 20, 2021,[7] November 19, 2021,[8] and January 7, 2022.[9] On January 31, 2022, FDA approved SPIKEVAX (COVID-19 Vaccine, mRNA)[10] and reissued the letter in its entirety for both Moderna COVID-19 Vaccine and certain uses of SPIKEVAX (COVID-19 Vaccine, mRNA).[11]

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[4] In the February 25, 2021 revision, FDA allowed flexibility on the date of submission of monthly periodic safety reports and revised the requirements for reporting of vaccine administration errors by ModernaTX, Inc.

[5] In the July 7, 2021 revision, FDA clarified terms and conditions that relate to export of Moderna COVID-19 Vaccine (Original monovalent) from the United States.

[6] In the August 12, 2021 revision, FDA authorized for emergency use a third dose of the Moderna COVID-19 vaccine (Original monovalent) administered at least 1 month following the two dose series of this vaccine in individuals 18 years of age or older who have undergone solid organ transplantation, or individuals 18 years of age or older who have been diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

[7] In the October 20, 2021 revision, FDA authorized for emergency use the administration of a single booster dose of Moderna COVID-19 Vaccine (Original monovalent) at least 6 months after completing the primary series of this vaccine in individuals: 65 years of age and older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2. Additionally, FDA authorized the administration of a single booster dose of the Moderna COVID-19 Vaccine (Original monovalent) as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster dose were the same as those authorized for a booster dose of the vaccine used for primary vaccination.

[8] In the November 19, 2021 revision, FDA authorized the use of Moderna COVID-19 Vaccine (Original monovalent) as a single booster dose in individuals 18 years of age or older at least 6 months after completing the primary series of this vaccine (i.e., as a homologous booster dose), and authorized the use of the vaccine as a single booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine (i.e., as a heterologous booster dose) in individuals 18 years of age or older. The dosing interval for the heterologous booster dose was authorized to be the same as that authorized for a booster dose of the vaccine used for primary vaccination.

[9] In the January 7, 2022 revision, FDA revised the authorized dosing interval of the homologous booster dose to at least five (5) months after completion of the primary series of Moderna COVID-19 Vaccine (Original monovalent). In addition, FDA revised the Fact Sheets for Healthcare Providers Administering Vaccine (Vaccination Providers) and the Fact Sheet for Recipients and Caregivers to reflect this revision.

[10] SPIKEVAX (COVID-19 Vaccine, mRNA) was approved for active immunization to prevent COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 18 years of age and older.

[11] In the January 31, 2022 revision, FDA clarified that, subsequent to the FDA approval of SPIKEVAX (COVID-19 Vaccine, mRNA) for the prevention of COVID-19 for individuals 18 years of age and older, this EUA would remain in place for the Moderna COVID-19 Vaccine (Original monovalent) for the previously-authorized uses. It also authorized SPIKEVAX (COVID-19 Vaccine, mRNA) under this EUA for certain uses that are not included in the approved Biologics License Application (BLA). In addition, the Fact Sheet for Recipients and Caregivers was updated as the Vaccine Information Fact Sheet for Recipients and Caregivers, which comprises the Fact Sheet for the authorized Moderna COVID-19 Vaccine (Original monovalent) and information about the FDA-licensed vaccine, SPIKEVAX (COVID-19 Vaccine, mRNA).

Subsequently, FDA reissued the letter of authorization on March 15, 2022,[12] March 29, 2022,[13] June 17, 2022,[14] and August 31, 2022.[15] The August 31, 2022 reissuance provided for certain emergency uses of the Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)[16] after either completion of primary vaccination with any FDA approved or authorized monovalent COVID-19 vaccine[17] or receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine.

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[12] In the March 15, 2022 revision, FDA changed the timing of periodic safety report submissions from monthly to every two months.

[13] In the March 29, 2022 revision, FDA authorized: 1) the administration of a second booster dose of SPIKEVAX (COVID-19 Vaccine, mRNA) or the Moderna COVID-19 Vaccine (Original monovalent) at least 4 months after receipt of a first booster dose of any FDA authorized or approved COVID-19 vaccine to: a) individuals 50 years of age and older; and b) individuals 18 years of age or older who have undergone solid organ transplantation, or individuals 18 years of age or older who have been diagnosed with conditions that are considered to have an equivalent level of immunocompromise; and 2) a manufacturing change to include an additional presentation of the Moderna COVID-19 Vaccine (Original monovalent) for booster vaccination doses only, supplied in multiple dose vials with dark blue caps and labels with a purple border.

[14] In the June 17, 2022 revision, FDA authorized the use of: SPIKEVAX (COVID-19 Vaccine, mRNA) or the Moderna COVID-19 Vaccine (Original monovalent) as: 1) a two-dose primary series for the prevention of COVID-19 in individuals 12 through 17 years of age; and 2) a third primary series dose at least 1 month following the second dose of this vaccine in individuals 12 through 17 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise. FDA also authorized the Moderna COVID-19 Vaccine (Original monovalent) as 1) a two-dose primary series for the prevention of COVID-19 in individuals 6 months through 11 years of age (6 months through 5 years of age, and 6 years through 11 years of age); and 2) a third primary series dose at least 1 month following the second dose of this vaccine in individuals 6 months through 11 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise. In addition, FDA authorized two new presentations of the Moderna COVID-19 Vaccine (Original monovalent): 1) multiple dose vials, with dark blue caps and labels with a magenta border, each 0.25 mL dose containing 25 mcg mRNA; and 2) multiple dose vials, with dark blue caps and labels with a teal border, each 0.5 mL dose containing 50 mcg mRNA. Finally, FDA authorized the use of the presentation of the Moderna COVID-19 Vaccine (Original monovalent) in multiple dose vials, with dark blue caps and labels with a purple border (each 0.5 mL dose containing 50 mcg mRNA), labeled "BOOSTER DOSES ONLY" to provide primary series doses in individuals 6 years through 11 years of age.

[15] In the August 31, 2022 revision, FDA authorized the use of Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) in multiple dose vials with dark blue caps and labels with gray borders (each 0.5 mL dose containing a total of 50 mcg mRNA) for the prevention of COVID-19 in individuals 18 years of age or older as a single booster dose administered at least 2 months after either: 1) completion of primary vaccination with any FDA authorized or approved monovalent COVID-19 vaccine, or 2) receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine. FDA also revised the scope of authorization for SPIKEVAX (COVID-19 Vaccine, mRNA) and Moderna COVID-19 Vaccine (Original monovalent) to remove their use as a booster dose for individuals 18 years of age and older. Finally, FDA revised the Fact Sheets for Moderna COVID-19 Vaccine (Original monovalent), as applicable, to reflect these changes and to reflect updates to the Conditions of Authorization regarding VAERS reporting.

[16] Hereinafter, this letter refers to this vaccine as the "Moderna COVID-19 Vaccine, Bivalent."

[17] For purposes of this letter, monovalent COVID-19 Vaccine refers to any COVID-19 Vaccine that contains or encodes the spike protein of only the Original SARS-CoV-2. We note that the Moderna COVID-19 Vaccine (2023-2024 Formula) is also monovalent and encodes the spike protein of SARS-CoV-2 Omicron variant lineage XBB 1.5.

Subsequently, FDA reissued the letter of authorization on October 12, 2022,[18] December 8, 2022,[19] and April 18, 2023.[20]

On September 11, 2023, FDA approved SPIKEVAX (COVID-19 Vaccine, mRNA) (2023-2024 Formula)[21] for active immunization to prevent COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 12 years of age and older and also

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[18] In the October 12, 2022 revision, FDA authorized Moderna COVID-19 Vaccine, Bivalent as a single booster dose in individuals 12 through 17 years of age and 6 through 11 years of age at least 2 months after either: 1) completion of primary vaccination with any FDA authorized or approved monovalent COVID-19 vaccine, or 2) receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine. For both of these age groups, FDA authorized the use of the Moderna COVID-19 Vaccine, Bivalent in multiple dose vials with dark blue caps and labels with gray borders. The authorized volume of the booster dose is age dependent. A single booster dose for individuals 12 through 17 years of age is a 0.5 mL dose containing a total of 50 mcg mRNA. A single booster dose for individuals 6 through 11 years of age is a 0.25 mL dose containing a total of 25 mcg mRNA. In addition, FDA revised the Fact Sheets for Moderna COVID-19 Vaccine, Bivalent to reflect these changes.

[19] In the December 8, 2022 revision, FDA authorized the use of Moderna COVID-19 Vaccine, Bivalent in multiple dose vials with dark pink caps and labels with a yellow box (each 0.2 mL dose containing a total of 10 mcg of mRNA) in individuals 6 months through 5 years of age at least 2 months after completion of primary vaccination with Moderna COVID-19 Vaccine. In addition, because another COVID-19 vaccine's primary series for individuals 6 months through 4 years of age was revised to no longer consist of only monovalent doses, FDA revised the scope of authorization for the Moderna COVID-19 Vaccine, Bivalent for use in individuals 6 years of age and older so that it can be administered as a booster dose regardless of whether primary vaccination was completed with a monovalent COVID-19 vaccine. Specifically, FDA authorized the Moderna COVID-19 Vaccine, Bivalent in multiple dose vials with dark blue caps and labels with gray borders for use in individuals 6 through 11 years of age (each 0.25 mL booster dose containing a total of 25 mcg mRNA) and for use in individuals 12 years of age and older (each 0.5 mL booster dose containing a total of 50 mcg mRNA) as a single booster dose administered at least 2 months after either: 1) completion of primary vaccination with any FDA authorized or approved COVID-19 vaccine, or 2) receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine. FDA revised the applicable Fact Sheets for Moderna COVID-19 Vaccine (Original monovalent), and the Fact Sheets for Moderna COVID-19 Vaccine, Bivalent, to reflect these changes. Finally, FDA revised the Fact Sheets for Moderna COVID-19 Vaccine (Original monovalent), and the Fact Sheets for Moderna COVID-19 Vaccine, Bivalent, to convey that urticaria has been reported during post-authorization use.

[20] In the April 18, 2023 revision, FDA: 1) revised the authorized dosing regimen and schedule of the Moderna COVID-19 Vaccine, Bivalent, as described in Section II of the April 18, 2023 reissuance of this letter; 2) no longer authorized use of the Moderna COVID-19 Vaccine and certain uses of SPIKEVAX (COVID-19 Vaccine; mRNA) in the United States; 3) clarified the terms and conditions that relate to export of Moderna COVID-19 Vaccine from the United States; and 4) revised Condition G to require the inclusion of distribution data for Moderna COVID-19 Vaccine and Moderna COVID-19 Vaccine, Bivalent in the monthly periodic safety reports. FDA also revised the applicable Fact Sheets for Moderna COVID-19 Vaccine, Bivalent, to reflect these changes. In addition, the Fact Sheets for Healthcare Providers Administering Vaccine (Vaccination Providers) were consolidated into a single Fact Sheet for Healthcare Providers Administering Vaccine for all authorized presentations of Moderna COVID-19 Vaccine, Bivalent; and the Fact Sheets for Recipients and Caregivers were consolidated into a single Fact Sheet for Recipients and Caregivers for all authorized presentations of Moderna COVID-19 Vaccine, Bivalent.

[21] SPIKEVAX (COVID-19 Vaccine, mRNA) (2023-2024 Formula) encodes the spike protein of SARS-CoV-2 Omicron variant lineage XBB.1.5 (Omicron XBB.1.5).

reissued this letter in its entirety.[22]

On August 22, 2024, FDA approved SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula)[23] for active immunization to prevent COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 12 years of age and older.

On August 22, 2024, having concluded that revising this EUA is appropriate to protect the public health or safety under section 564(g)(2) of the Act, FDA is reissuing the September 11, 2023 letter of authorization in its entirety with revisions to:

A. Authorize Moderna COVID-19 Vaccine (2024-2025 Formula)[24] in single dose pre-filled syringes (each 0.25 mL dose containing a total of 25 mcg of mRNA) for use in individuals 6 months through 11 years of age as described in Section II;
B. Authorize SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) for certain uses in certain immunocompromised individuals turning from 11 to 12 years of age during the vaccination series as described in Section II;
C. No longer authorize Moderna COVID-19 Vaccine (Original monovalent) for export from the United States;
D. No longer authorize Moderna COVID-19 Vaccine, Bivalent for export from the United States;
E. No longer authorize the use of the Moderna COVID-19 Vaccine (2023-2024 Formula) in the United States; and
F. Clarify the terms and conditions that relate to export of Moderna COVID-19 Vaccine (2023-2024 Formula) from the United States.

Additionally, FDA is authorizing the Fact Sheets for Moderna COVID-19 Vaccine (2024-2025 Formula) that reflect the relevant changes.

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[22] In the September 11, 2023 revision, FDA: 1) authorized Moderna COVID-19 Vaccine (2023-2024 Formula) in single dose vials with dark blue caps and labels with a green box (each 0.25 mL dose containing a total of 25 mcg of mRNA) for use in individuals 6 months through 11 years of age as described in Section II of the September 11, 2023 reissuance of this letter; 2) revised the conditions related to printed matter, advertising, and promotion to add additional requirements; 3) removed the requirement that distribution of vaccines authorized under this EUA must be distributed to emergency response stakeholders as directed by the U.S. Government and make corresponding changes to the Conditions of Authorization; 4) removed the requirement that vaccines authorized under this EUA be administered only by vaccination providers enrolled in the CDC COVID-19 Vaccination Program and make corresponding changes to the Conditions of Authorization; 5) revised Condition G to provide flexibility to determine a different reporting interval for periodic safety reports, if appropriate; 6) removed authorization for the use of the Moderna COVID-19 Vaccine, Bivalent in the United States; and 7) clarified the terms and conditions that relate to export of Moderna COVID-19 Vaccine, Bivalent from the United States. FDA also authorized the applicable Fact Sheets for Moderna COVID-19 Vaccine (2023-2024 Formula) that reflect the relevant changes.

[23] SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) encodes the spike protein of SARS-CoV-2 Omicron variant lineage KP.2.

[24] Moderna COVID-19 Vaccine (2024-2025 Formula) encodes the spike protein of SARS-CoV-2 Omicron variant lineage KP.2 (Omicron KP.2).

For the December 18, 2020 authorization for individuals 18 years of age and older, FDA reviewed safety and efficacy data from an ongoing phase 3 trial (Study 1) in approximately 30,000 participants randomized 1:1 to receive Moderna COVID-19 Vaccine (Original monovalent) or saline control. Study 1 enrolled participants 18 years of age and older. FDA's review of the available safety data from 30,351 participants 18 years of age and older, who were followed for a median of 7 weeks after receiving the second dose, did not identify specific safety concerns that would preclude issuance of an EUA. Review of additional safety data from these participants with a median of 9 weeks of follow-up after receipt of the second dose did not change FDA's assessment of safety of the vaccine. FDA's analysis of the efficacy data from 28,207 participants 18 years of age and older without evidence of SARS-CoV-2 infection prior to dose 1 confirms the vaccine was 94.1% effective (95% confidence interval (CI) 89.3, 96.8) in preventing COVID-19 occurring at least 14 days after the second dose (with 11 COVID-19 cases in the vaccine group compared to 185 COVID-19 cases in the placebo group). In this final scheduled analysis participants had been followed for a median of 9 weeks following the second dose. This result is consistent with that obtained from an interim analysis of efficacy conducted after these participants had been followed for a median of 7 weeks after the second dose (vaccine efficacy 94.5%, 95% CI: 86.5, 97.8). Based on the safety and effectiveness data, and review of manufacturing information regarding product quality and consistency, it is reasonable to believe that Moderna COVID-19 Vaccine (Original monovalent) may be effective. Additionally, it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Moderna COVID-19 Vaccine (Original monovalent) outweigh the known and potential risks of the vaccine, for the prevention of COVID-19 in individuals 18 years of age and older. Finally, on December 17, 2020, the Vaccines and Related Biological Products Advisory Committee voted in agreement with this conclusion.

For the August 12, 2021 authorization of a third primary series dose of the Moderna COVID-19 Vaccine (Original monovalent) in individuals 18 years of age or older who have undergone solid organ transplantation, or individuals 18 years of age or older who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise, FDA reviewed safety and effectiveness data reported in two manuscripts on solid organ transplant recipients. The first study was a double-blind, randomized-controlled study conducted in 120 individuals who had undergone various solid organ transplant procedures (heart, kidney, kidney-pancreas, liver, lung, pancreas) a median of 3.57 years earlier (range 1.99-6.75 years). A third dose of the Moderna COVID-19 vaccine (Original monovalent) was administered to 60 individuals approximately 2 months after they had received a second dose (i.e., doses at 0, 1 and 3 months); saline placebo was given to 60 individuals or comparison. The primary outcome was anti-RBD antibody at 4 months greater than 100 U/mL. This titer was selected based on NHP challenge studies as well as a large clinical cohort study to indicate this antibody titer was possibly protective. Secondary outcome was based on a virus neutralization assay polyfunctional T cell responses. Baseline characteristics were comparable between the two study arms as were pre-intervention anti-RBD titer and neutralizing antibodies. Levels of SARS-CoV-2 antibodies indicative of a significant response occurred four weeks after the third dose in 33/60 (55.0%) of the Moderna COVID-19 vaccinated group and 10/57 (17.5%) of the placebo individuals. In the 60 individuals who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 adverse events were reported. A supportive secondary study describes

a single arm study conducted in 101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) a median of 97±8 months earlier. A third dose of a similar messenger RNA COVID-19 vaccine, Pfizer-BioNTech COVID-19 Vaccine (Original monovalent), was administered to 99 of these individuals approximately 2 months after they had received a second dose. Levels of SARS-CoV-2 antibodies meeting the pre-identified criteria for success occurred four weeks after the third dose in 26/59 (44.0%) of those who were initially considered to be seronegative and received a third dose of the Pfizer-BioNTech COVID-19 Vaccine (Original monovalent); 67/99 (68%) of the entire group receiving a third vaccination had an increase in antibody titers that the investigators considered significant. In those who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported. Despite the moderate enhancement in antibody titers, the totality of data (including the supportive paper by Kamar et al. and demonstrated efficacy of the product in the elderly and persons with co-morbidities) supports the conclusion that a third dose of the Moderna COVID-19 Vaccine (Original monovalent) may be effective in this population, and that the known and potential benefit of a third dose of Moderna COVID-19 Vaccine (Original monovalent) outweigh the known and potential risks of the vaccine for immunocompromised individuals at least 18 years of age who have received two doses of the Moderna COVID-19 Vaccine (Original monovalent) and who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

For the October 20, 2021 authorization of a single booster dose of the Original monovalent Moderna COVID-19 Vaccine administered at least 6 months after completing the primary series in individuals: 65 years of age or older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2, FDA reviewed safety and effectiveness data from an ongoing Phase 2 trial in which 171 participants aged 18 years and older received a single 50 mcg booster dose (0.25 mL) of the Moderna COVID-19 Vaccine (Original monovalent) at least 6 months (range 5.8-8.5 months) after completion of the 100 µg primary series (two 0.5 mL doses, one month apart). Following the booster dose, the median follow-up time was 5.7 months. FDA's review of the currently available safety data did not identify specific safety concerns that would preclude issuance of an EUA. The effectiveness of the 50 µg booster dose (0.25 mL) of the Moderna COVID-19 Vaccine (Original monovalent) is based on an assessment of neutralizing antibody titers (ID50) against a pseudovirus expressing the SARS-CoV-2 Spike protein from a USA_WA1/2020 isolate carrying the D614G mutation. Immunogenicity analyses compared the ID50 one month after the booster dose in 149 participants to the ID50 one month after the primary series in a random subset of 1055 participants from another study. Participants from these two studies had no serologic or virologic evidence of SARS-CoV-2 infection prior to the booster dose and prior to the first primary series dose, respectively. FDA's analyses confirmed that the immunobridging criteria for a booster response were met for a comparison of the ID50 geometric mean titers and that the immunobridging criterion for a booster response was not met for a comparison of ID50 seroresponse rates. Based on the totality of the scientific evidence available, including data from the above-referenced clinical trials, FDA concluded that a booster dose of the Moderna COVID-19 Vaccine (Original monovalent) may be effective, and that the known and potential benefits of a single booster dose at least 6 months after completing the

primary series outweigh the known and potential risks for individuals 65 years of age and older, individuals 18 through 64 years of age at high risk of severe COVID-19, and individuals 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2.

For the October 20, 2021 authorization of a single booster dose of the Moderna COVID-19 Vaccine (Original monovalent) as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine, FDA reviewed data from an ongoing Phase1/2 clinical trial in participants 19-85 years of age. In this study, adults who had completed primary vaccination with Moderna COVID-19 Vaccine (Original monovalent) 2-dose series (N=151), a Janssen COVID-19 Vaccine single dose (N=156), or a Pfizer-BioNTech COVID-19 Vaccine (Original monovalent) 2-dose series (N=151) at least 12 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 (Original monovalent) (0.5 mL), Janssen COVID-19 Vaccine, or Pfizer-BioNTech COVID-19 Vaccine (Original monovalent). Adverse events were assessed through 28 days after the booster dose. An overall review of adverse reactions reported following the Moderna COVID-19 Vaccine (Original monovalent) heterologous booster dose (0.5 mL) did not identify any new safety concerns, as compared with adverse reactions reported following Moderna COVID-19 Vaccine (Original monovalent) primary series doses or homologous booster dose (0.25 mL). 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 (Original monovalent) 100 mcg (0.5 mL) was demonstrated regardless of primary vaccination. FDA also considered immunogenicity data from manufacturer-conducted clinical trials that evaluated both a 0.25 mL dose and a 0.5 mL dose of the Moderna COVID-19 Vaccine (Original monovalent) for the first dose of the primary series and a 0.25 mL dose for a homologous booster dose. Based on the totality of the scientific evidence available, including data from the above-referenced clinical trial, FDA concluded that a heterologous booster dose (0.25 mL) of the Moderna COVID-19 Vaccine (Original monovalent) may be effective, and that the known and potential benefits of a heterologous booster dose of the Moderna COVID-19 Vaccine (Original monovalent) following completion of primary vaccination with another authorized or approved COVID-19 vaccine outweigh the known and potential risks.

For the November 19, 2021 authorization expanding the eligible population for the homologous and heterologous booster doses to individuals 18 years of age and older, FDA reviewed data provided by the sponsor and other data available to FDA, including real world evidence. Data previously reviewed to support the October 20, 2021, authorization of a homologous booster dose, together with new real-world data indicating increasing COVID-19 cases in the United States, including among vaccinated individuals, and suggesting a decreased risk of myocarditis following mRNA COVID-19 vaccine booster doses compared with second primary series doses, supported expansion of the population eligible for a Moderna COVID-19 Vaccine (Original monovalent) homologous booster dose to include all individuals 18 years of age and older who completed the primary series at least 6 months previously. Data previously reviewed to support the October 20, 2021, authorization of a heterologous booster dose, together with data and

information to support authorization of the EUA amendment to expand the eligible population for a homologous booster dose of the Pfizer-BioNTech Vaccine (Original monovalent), support a revision to the Moderna COVID-19 Vaccine (Original monovalent) EUA such that the eligible population for a heterologous booster dose of the Moderna COVID-19 Vaccine (Original monovalent) is all adults 18 years of age and older who completed primary vaccination with another authorized or approved COVID-19 vaccine. Based on the totality of the scientific evidence available, FDA concluded that a homologous or heterologous booster dose of the Moderna COVID-19 Vaccine (Original monovalent) may be effective, and that the known and potential benefits of the booster dose of the Moderna COVID-19 Vaccine (Original monovalent) following completion of primary vaccination with Moderna COVID-19 Vaccine (Original monovalent) or another authorized or approved COVID-19 vaccine outweigh the known and potential risks in individuals 18 years of age and older.

For the January 7, 2022 authorization revising the authorized dosing interval of the homologous booster dose to at least 5 months after completion of the primary series with Moderna COVID-19 Vaccine (Original monovalent), the FDA reviewed: prepublications; accepted publications; published publications; and real world evidence on the safety of booster doses provided by the Israeli Ministry of Health, which includes data from approximately 4.1 million third (booster) doses of the Pfizer-BioNTech COVID-19 Vaccine (Original monovalent) given to individuals 16 years of age and older at least 5 months after the primary series with Pfizer-BioNTech COVID-19 Vaccine (Original monovalent), and which did not raise new safety concerns associated with the booster dose. Although the overall composition of the Moderna COVID-19 Vaccine (Original monovalent) is different than the Pfizer-BioNTech COVID-19 Vaccine (Original monovalent), both are mRNA vaccines with safety and efficacy profiles that, though not identical, are relatively similar. Acknowledging the differences, it is reasonable to make the inference that the safety data on the 5 month interval for booster doses obtained in the population in Israel can apply to the Moderna COVID-19 Vaccine (Original monovalent). Based on the totality of the scientific evidence available, FDA concluded that a homologous booster dose of the Moderna COVID-19 Vaccine (Original monovalent) may be effective and that the known and potential benefits of the booster dose of the Moderna COVID-19 Vaccine (Original monovalent) following completion of primary vaccination with the Moderna COVID-19 Vaccine (Original monovalent) outweigh the known and potential risks in individuals 18 years of age and older when given at least 5 months following the primary series.

For the March 29, 2022 authorization of a second booster dose of the Moderna COVID-19 Vaccine (Original monovalent) for administration to individuals 50 years of age and older and to individuals 18 years of age or older with certain kinds of immunocompromise at least 4 months after receipt of a first booster dose of any FDA authorized or approved COVID-19 vaccine, the sponsor provided a publication of an ongoing, open label, non-randomized study conducted in healthcare workers at a single site in Israel. (*Gili Regev-Yochay, Tal Gonen, Mayan Gilboa, et al. 2022 DOI: 10.1056/NEJMc2202542*). In this study, 120 individuals 18 years of age and older who had received primary vaccination and a first booster dose with Pfizer-BioNTech COVID-19 Vaccine (Original monovalent) were administered a second booster dose of Moderna COVID-19 Vaccine (Original monovalent) at least four months after the first booster dose. Among these individuals, approximately 7- to 16-fold increases in geometric mean neutralizing antibody titers

against wild-type virus and Delta and Omicron variants, were reported at two weeks after the second booster as compared to 5 months after the first booster dose. No new safety concerns were reported during up to three weeks of follow up after the second booster dose. Based on the totality of the scientific evidence available, FDA concluded that a second booster dose of the Moderna COVID-19 Vaccine (Original monovalent) may be effective and that the known and potential benefits of a second booster dose of the Moderna COVID-19 Vaccine (Original monovalent) following receipt of a first booster dose of any FDA authorized or approved COVID-19 vaccine outweigh the known and potential risks in the authorized populations when given at least 4 months following the first booster dose.

For the March 29, 2022 authorization of the manufacturing change to include an additional presentation of the Moderna COVID-19 Vaccine (Original monovalent) containing 50 mcg mRNA per 0.5 mL dose in a multiple dose vial presentation (supplied in a vial with a dark blue cap and a label with a purple border), FDA reviewed data on analytical comparability, which uses laboratory testing to demonstrate that a change in product manufacturing is not expected to impact safety or effectiveness. For the additional Moderna COVID-19 Vaccine (Original monovalent) presentation, the results of multiple different tests to assess critical quality attributes and safety were evaluated, including tests for appearance, lipid nanoparticle size, mRNA and lipid content and purity, sterility and endotoxin content. For this additional presentation, results of tests performed to assess critical safety and quality attributes and other characterization tests showed that the additional Moderna COVID-19 Vaccine (Original monovalent) presentation for use only for booster vaccination doses (supplied in a multiple dose vial with a dark blue cap and a label with a purple border) is expected to have the same safety and effectiveness as the currently authorized presentation (supplied in a multiple dose vial with a red cap and a label with a light blue border).

For the June 17, 2022 authorization of the Moderna COVID-19 Vaccine (Original monovalent) for individuals 6 months through 17 years of age, and the two new presentations of the Moderna COVID-19 Vaccine (Original monovalent), FDA reviewed safety and effectiveness data from two ongoing studies, Study 3 and Study 4. Study 3 is an ongoing Phase 2/3 trial that has enrolled 3,726 participants 12 through 17 years of age, of whom 2,486 participants received at least one dose of Moderna COVID-19 Vaccine (Original monovalent) (containing 100 mcg mRNA per dose) and 1,240 participants received saline placebo. Participants with a known history of SARS-CoV-2 infection were excluded from the study. FDA's review of the available safety data among 2,486 participants who received Moderna COVID-19 Vaccine (Original monovalent) and had a median follow-up duration of 53 days after the second dose for blinded, placebo-controlled follow-up and 312 days after the second dose including unblinded follow-up, did not identify specific safety concerns that would preclude issuance of an EUA. Effectiveness is based on a comparison of immune responses in this age group to adults 18 through 25 years of age. SARS-CoV-2 50% neutralizing antibody titers and seroresponse rates 28 days after the second dose were compared between a subset of participants 12 through 17 years of age from Study 3 and a subset of participants 18 through 25 years of age who received Moderna COVID-19 Vaccine (Original monovalent) (containing 100 mcg mRNA per dose) in the above-referenced Study 1. Participants included in these analyses had no immunologic or virologic evidence of prior SARS-CoV-2 at baseline. FDA's analyses confirm that immunobridging criteria were met for

both geometric mean antibody titers and seroresponse rates. FDA's analysis of available descriptive efficacy data from 3,181 participants 12 through 17 years of age who had a negative baseline SARS-CoV-2 status confirm that the vaccine was 93.3% effective (95% confidence interval 47.9, 99.9) in preventing COVID-19 (defined as at least one symptom of COVID-19 and a positive SARS-CoV-2 test). The median length of follow up for efficacy for participants in the study was 53 days post Dose 2. Study 4 is an ongoing Phase 2/3 trial that has enrolled 4,002 participants 6 years through 11 years of age, of whom 3,007 participants received at least one dose of Moderna COVID-19 Vaccine (Original monovalent) (50 mcg mRNA per dose) and 995 participants received saline placebo. Participants with a known history of SARS-CoV-2 infection within 2 weeks of study vaccination were excluded from the study. FDA's review of the available safety data among 3,007 participants who received Moderna COVID-19 Vaccine (Original monovalent) and had a median follow-up duration of 51 days after the second dose for blinded, placebo-controlled follow-up and 158 days after the second dose including unblinded follow-up, did not identify specific safety concerns that would preclude issuance of an EUA. Effectiveness in individuals 6 years through 11 years of age is based on a comparison of immune responses in this age group to adults 18 through 25 years of age. SARS-CoV-2 50% neutralizing antibody titers and seroresponse rates 28 days after the second dose were compared between a subset of participants 6 years through 11 years of age in this study to a subset of individuals 18 through 25 years of age who received Moderna COVID-19 Vaccine (Original monovalent) (containing 100 mcg mRNA) in Study 1. Participants included in these analyses had no immunologic or virologic evidence of prior SARS-CoV-2 at baseline. FDA's analyses confirm that immunobridging criteria were met for both geometric mean antibody titers and seroresponse rates. Safety and effectiveness of the Moderna COVID-19 Vaccine (Original monovalent) for individuals 6 months through 5 years of age were also evaluated in Study 4. In Study 4, 6,388 participants 6 months through 5 years of age were enrolled, of whom 4,792 received at least one dose of Moderna COVID-19 Vaccine (Original monovalent) (25 mcg mRNA per dose) and 1,596 received saline placebo. Among these participants, 4,038 participants (3,031 who received Moderna COVID-19 Vaccine (Original monovalent) and 1,007 who received placebo) were 2 through 5 years of age and 2,350 participants (1,761 who received Moderna COVID-19 Vaccine (Original monovalent) and 589 who received placebo) were 6 through 23 months of age. The median duration of blinded follow-up for safety was 71 days after Dose 2 for participants 2 through 5 years and 68 days after Dose 2 for participants 6 through 23 months of age. FDA's review of the available safety data among 4,038 participants 2 through 5 years of age and 2,350 participants 6 through 23 months of age did not identify specific safety concerns that would preclude issuance of an EUA. Effectiveness in individuals 6 months through 5 years of age is based on a comparison of immune responses in this age group to adults 18 through 25 years of age. SARS-CoV-2 neutralizing antibody concentrations and seroresponse rates 28 days after the second dose were compared between a subset of participants 2 through 5 years of age in Study 4 and a subset of participants 18 through 25 years of age in Study 1, and between a subset of participants 6 through 23 months in Study 4 and a subset of participants 18 through 25 years of age in Study 1. Participants included in these analyses had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. FDA's analyses confirm that for both age groups, 2 through 5 years and 6 through 23 months, immunobridging criteria were met for both geometric mean antibody concentrations and seroresponse rates. FDA's analysis of available descriptive efficacy data from 5,476 participants 6 months through 5 years of age show that the vaccine was

36.8% effective (95% confidence interval 12.5, 54.0) in preventing COVID-19 (defined as at least one symptom of COVID-19 and a positive SARS-CoV-2 test) in individuals 2 through 5 years of age and 50.6% effective (95% confidence interval 21.4, 68.6) in individuals 6 through 23 months of age. The median length of follow-up for efficacy post-Dose 2 was 71 days for participants 2 through 5 years of age and 68 days for participants 6 through 23 months of age. Based on these data, FDA concluded that it is reasonable to believe that Moderna COVID-19 Vaccine (Original monovalent) may be effective in individuals 6 months through 17 years of age. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Moderna COVID-19 Vaccine (Original monovalent) outweigh the known and potential risks of the vaccine for the prevention of COVID-19 in individuals 6 months through 17 years of age. On June 14, 2022, the Vaccines and Related Biological Products Advisory Committee voted in agreement with this conclusion for individuals 6 through 17 years. On June 15, 2022, the Vaccines and Related Biological Products Advisory Committee voted in agreement with this conclusion for individuals 6 months through 5 years of age.

For the June 17, 2022 authorization of a third primary series dose of Moderna COVID-19 Vaccine (Original monovalent) in individuals 6 months through 17 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise, safety in this population is extrapolated from the experience in children 6 months through 17 years of age who were vaccinated with a 2-dose primary series and the above mentioned safety data on a third primary series dose of the Moderna COVID-19 Vaccine (Original monovalent) in adult solid organ transplant recipients. Effectiveness in this population is extrapolated from available immunogenicity and efficacy data on a 2-dose primary series in individuals in this age group and adults and the above mentioned effectiveness data on a third primary series dose of the Moderna COVID-19 Vaccine (Original monovalent) in adult solid organ transplant recipients. Based on the totality of the scientific evidence available, FDA concluded that a third dose of the Moderna COVID-19 Vaccine (Original monovalent) may be effective and that the known and potential benefits of a third dose of the Moderna COVID-19 Vaccine (Original monovalent) outweigh the known and potential risks of the vaccine for immunocompromised individuals 6 months through 17 years of age who have received two doses of the Moderna COVID-19 Vaccine (Original monovalent) and who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

The August 31, 2022 authorization of a booster dose of the Moderna COVID-19 Vaccine, Bivalent, in individuals 18 years of age and older is based on: 1) safety and effectiveness data from clinical trials which evaluated primary and booster vaccination with Moderna COVID-19 Vaccine (Original monovalent); 2) postmarketing safety data with Moderna COVID-19 Vaccine (Original monovalent); and 3) safety and immunogenicity data from a clinical trial (Study 5) which evaluated a booster dose of Moderna's bivalent COVID-19 vaccine (Original and Omicron BA.1), not authorized or approved in the U.S., hereafter referred to as bivalent vaccine (Original and Omicron BA.1). FDA considered safety and effectiveness data previously reviewed by FDA in support of the December 18, 2020 and June 17, 2022 authorizations of primary vaccinations and the October 20, 2021, November 19, 2021, January 7, 2022, and March

29, 2022 authorizations of booster vaccinations in individuals 18 years and older with Moderna COVID-19 Vaccine (Original monovalent), as well as postmarketing safety data. Study 5 is a Phase 2/3 open-label study that evaluated the immunogenicity, safety, and reactogenicity of a booster dose of the bivalent vaccine (Original and Omicron BA.1) compared to a booster dose of Moderna COVID-19 Vaccine (Original monovalent) when administered as a second booster dose to participants 18 years of age and older who had previously received a primary series and a first booster dose with Moderna COVID-19 Vaccine (Original monovalent) at least 3 months prior. The safety analysis set included 437 participants in the bivalent vaccine (Original and Omicron BA.1) booster dose group and 377 participants in the Moderna COVID-19 Vaccine (Original monovalent) booster dose group. Following the booster dose through the cutoff date of April 27, 2022, the median follow-up time was 43 days among bivalent vaccine (Original and Omicron BA.1) recipients and 57 days among Moderna COVID-19 Vaccine (Original monovalent) recipients. FDA's review of the safety data accrued with the bivalent vaccine (Original and Omicron BA.1) together with the previously submitted safety data from clinical trials and postmarketing safety data with Moderna COVID-19 Vaccine (Original monovalent) did not identify specific safety concerns that would preclude issuance of an EUA. In Study 5, primary immunogenicity analyses evaluated 50% inhibitory dose (ID50) neutralizing antibody geometric mean titers (GMTs) and seroresponse rates (the proportion achieving a ≥4-fold rise in ID50 from pre-dose 1 of the primary series) 28 days following a second booster dose with bivalent vaccine (Original and Omicron BA.1) relative to those following a second booster dose with Moderna COVID-19 Vaccine (Original monovalent). Primary analyses of GMTs met predefined success criteria for superiority against Omicron BA.1 and noninferiority against the Original strain. The primary analysis of seroresponse against Omicron BA.1 met the criterion for noninferiority. Post-hoc analyses evaluated seroresponse rates (the proportion achieving a ≥4-fold rise in ID50 from pre-second booster) against both the Original strain and Omicron BA.1. The lower limit of the 2-sided 97.5% CI for the percentage difference in seroresponse rate (bivalent vaccine [Original and Omicron BA.1] minus Moderna COVID-19 Vaccine (Original monovalent)) was 12.9 against Omicron BA.1 and 2.1 against the Original strain. Based on the totality of the scientific evidence available, including these data and previously submitted data on the effectiveness of primary and booster vaccination with Moderna COVID-19 Vaccine (Original monovalent) in individuals 18 years of age and older, FDA concluded that it is reasonable to believe that Moderna COVID-19 Vaccine, Bivalent may be effective as a booster dose in individuals 18 years of age and older when administered at least 2 months after completion of primary vaccination or receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Moderna COVID-19 Vaccine, Bivalent outweigh the known and potential risks of the vaccine for the prevention of COVID-19 in individuals 18 years of age and older when administered at least 2 months after completion of primary vaccination or receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine. In addition, authorization of Moderna COVID-19 Vaccine, Bivalent was considered for the express purpose of improving protection conferred by COVID-19 vaccine booster doses against the currently circulating Omicron variant of SARS-CoV-2, resulting in a more favorable anticipated benefit/risk balance compared to Moderna COVID-19 Vaccine (Original monovalent). Consequently, revising this EUA to no longer provide for the use of the Moderna

COVID-19 Vaccine (Original monovalent) as a booster dose was appropriate for the protection of public health.

The October 12, 2022 authorization of a booster dose of Moderna COVID-19 Vaccine, Bivalent in individuals 6 years through 17 years of age is based on the data that FDA relied on for the August 31, 2022 authorization of the Moderna COVID-19 Vaccine, Bivalent in individuals 18 years of age and older. In addition, FDA reviewed data regarding the use of Moderna COVID-19 Vaccine (Original monovalent) as a booster dose in individuals 6 years through 11 years of age and 12 through 17 years of age. Safety and effectiveness data for a booster dose of Moderna COVID-19 Vaccine (Original monovalent) in individuals 12 through 17 years of age were collected in Study 3, an ongoing Phase 2/3 clinical trial described above. The open-label booster portion of the study involved 1,364 participants 12 years through 17 years of age who received a booster dose of Moderna COVID-19 Vaccine (Original monovalent) at least 5 months after the second dose of the primary series. As of the data cutoff date, the median duration of follow-up for safety was 116 days after the booster dose. FDA's review of the safety data from the open-label booster portion of Study 3 did not identify specific safety concerns that would preclude issuance of an EUA. Effectiveness of a booster dose of the Moderna COVID-19 Vaccine (Original monovalent) in participants 12 years through 17 years of age was based on a comparison of immune responses, as assessed by neutralizing antibody concentration against a pseudovirus expressing the SARS-CoV-2 Spike protein from a USA_WA1/2020 isolate carrying the D614G mutation, following the booster dose in this age group to that following the primary series in adults 18 through 25 years. The primary immunogenicity analysis population included 257 booster dose participants in Study 3 and a random subset of 295 participants 18 through 25 years from Study 1 (described above) who received two doses of Moderna COVID-19 Vaccine (Original monovalent) 1 month apart. Study 1 and 3 participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively. The primary immunogenicity analyses of the GMC ratio and difference in seroresponse rates following the booster dose in Study 3 compared to after the primary series in Study 1 met the pre-defined immunobridging success criteria. Seroresponse for a participant was defined as achieving a ≥4-fold rise of neutralizing antibody concentration from baseline (before the first dose of the primary series in Study 1 and Study 3). Safety and effectiveness data for a booster dose of Moderna COVID-19 Vaccine (Original monovalent) in individuals 6 years though 11 years of age were collected in Study 4, an ongoing Phase 2/3 clinical trial described above. The open-label booster portion of this study involved 1,294 participants 6 years through 11 years of age who received a booster dose of Moderna COVID-19 Vaccine (Original monovalent) at least 6 months after the second dose of the primary series. As of the data cutoff date, the median duration of follow-up for safety was 29 days after the booster dose. FDA's review of the safety data from the open-label booster portion of Study 4 did not identify specific safety concerns that would preclude issuance of an EUA. Effectiveness of a booster dose of the Moderna COVID-19 Vaccine (Original monovalent) in participants 6 years through 11 years of age was based on a comparison of immune responses, as assessed by neutralizing antibody concentration against a pseudovirus expressing the SARS-CoV-2 Spike protein from a USA_WA1/2020 isolate carrying the D614G mutation, following the booster dose in this age group to that following the primary series in adults 18 through 25 years. The primary immunogenicity analysis population included 95 booster dose participants in

Study 4 and a random subset of 295 participants 18 through 25 years from Study 1 who received two doses of Moderna COVID-19 Vaccine (Original monovalent) 1 month apart. Study 1 and 4 participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively. The primary immunogenicity analyses of the GMC ratio and difference in seroresponse rates following the booster dose in Study 4 compared to following the primary series in Study 1 met the pre-defined immunobridging success criteria. Seroresponse for a participant was defined as achieving a ≥4-fold rise of neutralizing antibody concentration from baseline (before the first dose of the primary series in Study 4 and Study 1). Based on the totality of the scientific evidence available, FDA concluded that it is reasonable to believe that Moderna COVID-19 Vaccine, Bivalent may be effective as a booster dose in individuals 6 years through 17 years of age when administered at least 2 months after completion of primary vaccination or receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Moderna COVID-19 Vaccine, Bivalent outweigh the known and potential risks of the vaccine for the prevention of COVID-19 in individuals 6 years through 17 years of age when administered at least 2 months after completion of primary vaccination or receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine.

The December 8, 2022 authorization of a booster dose of Moderna COVID-19 Vaccine, Bivalent in individuals 6 months through 5 years of age is based on data that FDA relied on for the August 31, 2022 authorization of the Moderna COVID-19 Vaccine, Bivalent in individuals 18 years of age and older. In addition, FDA reviewed postmarketing safety data with Moderna COVID-19 Vaccine (Original monovalent) and Moderna COVID-19 Vaccine, Bivalent, and safety and immunogenicity data regarding the use of the Moderna COVID-19 Vaccine (Original monovalent) as a booster dose in individuals 17 months through 5 years of age collected in Study 4. Study 4 is an ongoing Phase 2/3 Study with multiple parts. The open-label booster portion of the study involved 145 participants 17 months through 5 years of age who received a booster dose of Moderna COVID-19 Vaccine (Original monovalent) (10 mcg mRNA) at least 6 months after the completion of the Moderna COVID-19 Vaccine (Original monovalent) two-dose primary series. As of the data cutoff date of August 18, 2022, the median duration of follow-up for safety after the booster dose was 99 days. The primary immunogenicity analysis population included 56 booster dose participants in Study 4 and a random subset of 295 participants 18 through 25 years from Study 1 who had completed primary vaccination with two doses of Moderna COVID-19 Vaccine (Original monovalent) (100 mcg mRNA per dose) 1 month apart. Study 1 and 4 participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively. The primary immunogenicity analyses of the GMC ratio and difference in seroresponse rates following the booster dose in Study 4 compared to following the primary series in Study 1 met the pre-defined immunobridging success criteria. Seroresponse for a participant was defined as achieving a ≥4-fold rise of neutralizing antibody concentration from baseline (before the first dose of the primary series in Study 4 and Study 1). In a descriptive analysis, the booster dose seroresponse rate among participants 17 months through 5 years of age with seroresponse defined as at least a 4-fold rise relative to the pre-booster concentration, was

94.6%. The difference in seroresponse rates (Study 4 participants minus Study 1 participants) in this post-hoc analysis was -4.7% (95% CI -14.0, -0.9). Based on the totality of the scientific evidence available, FDA concluded that it is reasonable to believe that Moderna COVID-19 Vaccine, Bivalent may be effective as a booster dose in individuals 6 months through 5 years of age when administered at least 2 months after completion of primary vaccination with Moderna COVID-19 Vaccine (Original monovalent). Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Moderna COVID-19 Vaccine, Bivalent outweigh the known and potential risks of the vaccine for the prevention of COVID-19 in individuals 6 months through 5 years of age when administered at least 2 months after completion of primary vaccination with Moderna COVID-19 Vaccine (Original monovalent).

For the April 18, 2023 authorization, the effectiveness of Moderna COVID-19 Vaccine, Bivalent for individuals 6 months of age and older is based on previously reviewed data on 1) effectiveness of Moderna COVID-19 Vaccine (Original monovalent) and 2) immunogenicity of the bivalent vaccine (Original and Omicron BA.1). The effectiveness of a single dose of Moderna COVID-19 Vaccine, Bivalent for most individuals 6 years of age and older is based on seroprevalence surveys that estimate that almost all of the U.S. population 5 years of age and older now have antibodies (from vaccination and/or infection) against SARS-CoV-2 (*Centers for Disease Control and Prevention. COVID Data Tracker. Atlanta, GA: US Department of Health and Human Services, CDC; 2023, March 31. https://covid.cdc.gov/covid-data-tracker*) and a comparison of neutralizing antibody titers against a pseudovirus expressing the original SARS-CoV-2 Spike protein (D614G) at baseline (pre-Dose 1), at 28 days after Dose 1 for participants with evidence of prior SARS-CoV-2 infection, and at 28 days after Dose 2 for participants without evidence of prior SARS-CoV-2 infection. These data are from Study 4 and Study 1 evaluating a primary series of Moderna COVID-19 Vaccine (Original monovalent) for the following age groups: 6 years through 11 years of age and 18 years of age and older, respectively. In both age groups, neutralizing antibody titers at 28 days post-Dose 1 in participants with evidence of prior infection were not statistically different from those of participants without evidence of prior infection at 28 days post-Dose 2. The safety of Moderna COVID-19 Vaccine, Bivalent in individuals 6 months of age and older is based on previously reviewed safety data from clinical studies which evaluated primary and booster vaccination with Moderna COVID-19 Vaccine (Original monovalent), and a booster dose of bivalent vaccine (Original and Omicron BA.1); and postmarketing safety data with Moderna COVID-19 Vaccine (Original monovalent) and Moderna COVID-19 Vaccine, Bivalent. FDA's review of the available safety data in individuals 6 months of age and older did not identify specific safety concerns that would preclude issuance of an EUA. Based on the totality of the scientific evidence available, FDA concluded that it is reasonable to believe that Moderna COVID-19 Vaccine, Bivalent may be effective in individuals 6 months of age and older for the prevention of COVID-19 when administered in accordance with the revised dosing regimen and schedule. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Moderna COVID-19 Vaccine, Bivalent when administered in accordance with the revised dosing regimen and schedule outweigh the known and potential risks of the vaccine for the prevention of COVID-19 in individuals 6 months of age and older. The revised dosing regimen and schedule are set forth in the Scope of Authorization

(Section II). In addition, simplification of the vaccine composition (i.e., single vaccine composition for all doses) and schedule was considered for the express purpose of reducing complexity, decreasing vaccine administration errors due to the complexity of the number of different vial presentations, and potentially increasing vaccine uptake by allowing clearer communication. Revising the EUA to provide for a simplified vaccine composition and schedule in the United States, by no longer providing for the use of Moderna COVID-19 Vaccine (Original monovalent) in the United States, is appropriate for the protection of the public health.

The September 11, 2023 authorization of Moderna COVID-19 Vaccine (2023-2024 Formula) for individuals 6 months through 11 years of age is based on: 1) the effectiveness of the Moderna COVID-19 Vaccine (Original monovalent) in individuals 6 months of age and older, 2) the immunogenicity of Moderna COVID-19 Vaccine (Original and Omicron BA.1) in individuals 18 years of age and older, and 3) safety data previously reviewed. FDA's review of previously submitted safety data with Moderna COVID-19 Vaccine (Original monovalent) and Moderna COVID-19 Vaccine (Original and Omicron BA.1) and postmarketing safety data with Moderna COVID-19 Vaccine (Original monovalent) and Moderna COVID-19 Vaccine, Bivalent did not identify specific safety concerns that would preclude issuance of an EUA. The safety data accrued with the Moderna COVID-19 Vaccine (Original monovalent), bivalent vaccine (Original and Omicron BA.1) and Moderna COVID 19 Vaccine, Bivalent are relevant to Moderna COVID 19 Vaccine (2023-2024 Formula) because these vaccines are manufactured using the same process. Based on the totality of the scientific evidence available, FDA concluded that it is reasonable to believe that Moderna COVID-19 Vaccine (2023-2024 Formula) may be effective in individuals 6 months through 11 years of age for the prevention of COVID-19 when administered in accordance with the dosing regimen and schedule outlined in Section II. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of the Moderna COVID-19 Vaccine (2023-2024 Formula) outweigh the known and potential risks of the vaccine for the prevention of COVID-19 in individuals 6 months through 11 years of age when administered according to the authorized dosing regimen and schedule.

The August 22, 2024 authorization of Moderna COVID-19 Vaccine (2024-2025 Formula) for individuals 6 months through 11 years of age is based on: 1) Clinical safety, immunogenicity, and efficacy data from studies which evaluated primary series and booster vaccination with the Moderna COVID-19 Vaccine (Original monovalent) and Bivalent Vaccine (Original and Omicron BA.1), 2) Postmarketing safety surveillance data of Moderna COVID-19 Vaccine (Original monovalent), Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5), and Moderna COVID-19 Vaccine (2023-2024 Formula), 3) Nonclinical data demonstrating that Moderna COVID-19 Vaccine (2024-2025 Formula) when administered to vaccine-naive and vaccine-experienced laboratory animals, elicited higher neutralizing antibodies compared with the Moderna COVID-19 Vaccine (2023-2024 Formula) against JN.1-lineage descendant variants, 4) Chemistry, Manufacturing and Control information related to pre-filled syringe presentation of Moderna COVID-19 Vaccine (2024-2025 Formula), including but not limited to the manufacturing facilities. Based on the totality of the scientific evidence available, FDA concluded that it is reasonable to believe that Moderna COVID-19 Vaccine (2024-2025 Formula) may be effective in individuals 6 months through 11 years of age for the

prevention of COVID-19 when administered in accordance with the dosing regimen and schedule outlined in Section II. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of the Moderna COVID-19 Vaccine (2024-2025 Formula) outweigh the known and potential risks of the vaccine for the prevention of COVID-19 in individuals 6 months through 11 years of age when administered according to the authorized dosing regimen and schedule.

The August 22, 2024 authorization of SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) for use to complete the three-dose series on or after the date the individual with certain kinds of immunocompromise turns 12 years of age, is based on data previously reviewed to support 1) the August 12, 2021 authorization of Moderna COVID-19 Vaccine (Original monovalent) as a third primary series dose in individuals 18 years of age and older with certain kinds of immunocompromise and 2) the June 17, 2022 authorization of Moderna COVID-19 Vaccine (Original monovalent) as a two-dose primary series in individuals 6 months through 17 years of age. Based on the totality of the scientific evidence available, FDA concluded that it is reasonable to believe that SPIKEVAX (2024-2025 Formula) may be effective in individuals with certain kinds of immunocompromise turning from 11 to 12 years of age during the vaccination series for the prevention of COVID-19 when administered in accordance with the dosing regimen and schedule outlined in Section II. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of SPIKEVAX (2024-2025 Formula) outweigh the known and potential risks of the vaccine for the prevention of COVID-19 in individuals with certain kinds of immunocompromise turning from 11 to 12 years of age during the vaccination series when administered according to the authorized dosing regimen and schedule.

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of Moderna COVID-19 Vaccine (2024-2025 Formula), Moderna COVID-19 Vaccine (2023-2024 Formula), and SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) for the prevention of COVID-19, as described in the Scope of Authorization section (Section II) and subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of Moderna COVID-19 Vaccine (2024-2025 Formula)[25] for the prevention of COVID-19 when administered as described in the Scope of Authorization (Section II) meets the criteria for issuance of an authorization under Section 564(c) of the Act, because:

[25] In this section (Section I), references to Moderna COVID-19 Vaccine (2024-2025 Formula) also apply to Moderna COVID-19 Vaccine (2023-2024 Formula) and SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula).

A. SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;

B. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that Moderna COVID-19 Vaccine (2024-2025 Formula) may be effective in preventing COVID-19, and that, when used under the conditions described in this authorization, the known and potential benefits of Moderna COVID-19 Vaccine (2024-2025 Formula) when used to prevent COVID-19 outweigh its known and potential risks; and

C. There is no adequate, approved, and available alternative[26] to the emergency use of Moderna COVID-19 Vaccine (2024-2025 Formula) to prevent COVID-19.[27]

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited as follows:

- ModernaTX, Inc. will supply Moderna COVID-19 Vaccine (2024-2025 Formula) and Moderna COVID-19 Vaccine (2023-2024 Formula), either directly or through authorized distributor(s)[28] for use consistent with the terms and conditions of this EUA;
- Moderna COVID-19 Vaccine (2024-2025 Formula) and Moderna COVID-19 Vaccine (2023-2024 Formula) may be administered by a vaccination provider[29] without an individual prescription for each vaccine recipient;[30] and
- The Moderna COVID-19 Vaccine (2024-2025 Formula) and Moderna COVID-19 Vaccine (2023-2024 Formula), covered by this authorization, as described in more detail under *Product Description*, will be administered by vaccination providers in accordance with the uses described in the Scope of Authorization (Section II).

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[26] There are no COVID-19 vaccines that are approved to provide additional doses to certain immunocompromised populations as described in this EUA or COVID-19 vaccination in individuals younger than 12 years of age.

[27] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

[28] "Authorized Distributor(s)" are identified by ModernaTX, Inc. as an entity or entities allowed to distribute authorized Moderna COVID-19 Vaccine (2024-2025 Formula) or Moderna COVID-19 Vaccine (2023-2024 Formula)

[29] For purposes of this letter, "vaccination provider" refers to the facility, organization, or healthcare provider (e.g., non-physician healthcare professionals, such as nurses, pharmacists) licensed or otherwise authorized to administer or provide vaccination services pursuant to State law. If the vaccine is exported from the United States, a "vaccination provider" is a provider that is authorized to administer this vaccine in accordance with the laws of the country in which it is administered. For purposes of this letter, "vaccination provider" also includes a person authorized by the U.S. Department of Health and Human Services (e.g., under the PREP Act Declaration for Medical Countermeasures against COVID-19) to administer FDA-authorized COVID-19 vaccine (e.g., qualified pharmacy technicians and State-authorized pharmacy interns acting under the supervision of a qualified pharmacist). See, e.g., HHS, *Eleventh Amendment to the Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19 and Republication of the Declaration*. (88 FR 30769, May 12, 2023). In addition, for purposes of this letter, the term "State" includes any State or Territory of the United States, the District of Columbia, and the Commonwealth of Puerto Rico. See Section 201(a)(1) of the Act.

[30] When used under this EUA, SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) may be administered by a vaccination provider without an individual prescription for each vaccine recipient.

Table 1. Authorized Uses of Moderna COVID-19 Vaccine (2024-2025 Formula) for use in Individuals 6 Months Through 4 Years of Age

Number of Previous Doses with a Moderna COVID-19 Vaccine*	Dosing Regimen, Dose, and Schedule€
0^	2 doses¥, 0.25 mL each Dose 1: month 0 Dose 2: month 1
1	Single dose, 0.25 mL One month after receipt of a previous dose of Moderna COVID-19 Vaccine*
≥ 2	Single dose, 0.25 mL ≥ 2 months after receipt of the last previous dose of Moderna COVID-19 Vaccine*

* Previous dose refers to a dose of any prior Moderna COVID-19 Vaccine that is no longer authorized for use in the United States.
€ For individuals with certain kinds of immunocompromise previously vaccinated with a Moderna COVID-19 vaccine, see text following the tables for dosing information.
^ Not previously vaccinated with any COVID-19 vaccine
¥ Individuals turning from 4 years to 5 years of age during the vaccination series should receive both doses with Moderna COVID-19 Vaccine (2024-2025 Formula).

Table 2. Authorized Uses of the Moderna COVID-19 Vaccine (2024-2025 Formula) in Individuals 5 through 11 Years of Age Irrespective of COVID-19 Vaccination Status

Dosing Regimen, Dose and Schedule[a]
Single dose, 0.25 mL (If previously vaccinated, administer the dose ≥ 2 months after receipt of the last previous dose of COVID-19 vaccine [b])

[a] For individuals with certain kinds of immunocompromise, see text below tables for dosing information.
[b] Previous dose refers to a dose of any prior COVID-19 vaccine that is no longer authorized for use in the United States.

Individuals 6 Months through 11 Years of Age with Certain Kinds of Immunocompromise

The Moderna COVID-19 Vaccine (2024-2025 Formula) is authorized for use in individuals 6 months through 11 years of age with certain kinds of immunocompromise[31] according to the following dosing regimen and schedule:

[31] Certain kinds of immunocompromise refers to individuals who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Complete at least a three-dose series with a COVID-19 vaccine, each dose one month apart,[32] in which at least 1 dose is with a COVID-19 vaccine (2024-2025 Formula).

- If previously not vaccinated, complete the three-dose series with Moderna COVID-19 Vaccine (2024-2025 Formula).
- If previously vaccinated with one or two dose(s) of any prior formula of Moderna COVID-19 Vaccine,[33] complete the remaining dose(s) in the three-dose series with the Moderna COVID-19 Vaccine (2024-2025 Formula).
- If previously vaccinated with three or more doses of any prior formula of COVID-19 vaccines,[34] administer a single dose of Moderna COVID-19 Vaccine (2024-2025 Formula) at least two months following the last dose.

An additional dose of Moderna COVID-19 Vaccine (2024-2025 Formula) may be administered at least 2 months following the last dose of a COVID-19 vaccine (2024-2025 Formula).[35,36] Additional doses of Moderna COVID-19 Vaccine (2024-2025 Formula) may be administered at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances. The timing of the additional doses may be based on the individual's clinical circumstances.

Moderna COVID-19 Vaccine (2023-2024 Formula)

The Moderna COVID-19 Vaccine (2023-2024 Formula) is no longer authorized for use in the United States. However, the authorized presentation of the Moderna COVID-19 Vaccine (2023-2024 Formula) described in Section II of the September 11, 2023 reissuance of this Letter

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[32] COVID-19 vaccine, each dose of the three-doses series given one month apart, refers to Moderna COVID-19 vaccines. For individuals with certain kinds of immunocompromise turning from 11 years to 12 years of age during the vaccination series, SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) is authorized to complete the 3-dose series with 1 or 2 doses, as applicable, on or after the date the individual turns 12 years of age. Accordingly, after the individual turns 12 years of age, the vaccination series is completed with SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula), not Moderna COVID-19 Vaccine (2024-2025 Formula). Although SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) is approved for certain uses in individuals 12 years of age and older, if the individual turning 12 years of age receives 2 doses of the SPIKEVAX vaccine to complete the vaccination series or receives a dose of the SPIKEVAX vaccine less than 2 months after receipt of the last previous dose of COVID-19 vaccine to complete the vaccination series, then those uses of the SPIKEVAX vaccine are authorized under EUA.

[33] These prior COVID-19 vaccines are no longer authorized for use in the U.S.

[34] These prior COVID-19 vaccines are no longer authorized for use in the U.S.

[35] For immunocompromised individuals 6 months through 4 years of age, the last dose of a COVID-19 vaccine (2024-2025 Formula) refers to a dose with Moderna COVID-19 Vaccine (2024-2025 Formula).

[36] For immunocompromised individuals 5 years through 11 years of age, the last dose of a COVID-19 vaccine (2024-2025 Formula) refers to a dose with Pfizer-BioNTech COVID-19 Vaccine (2024-2025 Formula) or Moderna COVID-19 Vaccine (2024-2025 Formula).

remains authorized when exported from the United States in accordance with Section **III.** X. Under Section III.X, the Fact Sheets for Moderna COVID-19 Vaccine (2023-2024 Formula) that were authorized as of September 11, 2023 (Fact Sheet for Recipients and Caregivers) and as of November 1, 2023 (Fact Sheet for Healthcare Providers Administering Vaccine), and that describe the scope of FDA's September 11, 2023 authorization must, upon request, be made available to the regulatory authorities of the country in which the vaccine will be used.

Product Description[37]

The Moderna COVID-19 Vaccine (2024-2025 Formula) is provided in pre-filled syringes:

> Each 0.25 mL dose of Moderna COVID-19 Vaccine (2024-2025 Formula) supplied in a single dose pre-filled syringe contains 25 mcg mRNA encoding the pre-fusion stabilized S glycoprotein of the SARS-CoV-2 Omicron variant lineage KP.2. Each dose also contains the following ingredients: a total lipid content of 0.5 mg (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), 0.13 mg tromethamine, 0.62 mg tromethamine hydrochloride, 0.011 mg acetic acid, 0.049 mg sodium acetate trihydrate, and 21.8 mg sucrose. The Moderna COVID-19 Vaccine (2024-2025 Formula) does not contain a preservative.

The manufacture of the authorized Moderna COVID-19 Vaccine (2024-2025 Formula) is limited to those facilities identified and agreed upon in the ModernaTX, Inc. request for authorization.

For Moderna COVID-19 Vaccine (2023-2024 Formula) Section III.X refers to the Fact Sheets for Moderna COVID-19 Vaccine (2023-2024 Formula) that were authorized on September 11, 2023 (Fact Sheet for Recipients and Caregivers) and November 1, 2023 (Fact Sheet for Healthcare Providers Administering Vaccine). Those Fact Sheets describe the presentation of the Moderna COVID-19 Vaccine (2023-2024 Formula) that was authorized for use in the United States as of September 11, 2023 and that remains authorized for export in accordance with Section III.X.

The Moderna COVID-19 Vaccine (2024-2025 Formula) pre-filled syringe labels and carton labels and the Moderna COVID-19 Vaccine (2023-2024 Formula) vial labels and carton labels are clearly marked for use under "Emergency Use Authorization" or "EUA." The Moderna COVID-19 Vaccine (2024-2025 Formula) and Moderna COVID-19 Vaccine (2023-2024 Formula) are authorized to be distributed, stored, further redistributed, and administered when

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[37] For SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) description, see the SPIKEVAX (COVID-19 Vaccine, mRNA) prescribing information, found here: https://www.fda.gov/vaccines-blood-biologics/spikevax

packaged in the authorized manufacturer packaging (i.e., the pre-filled syringes or vials and the cartons), despite the fact that the pre-filled syringe or vial labels and carton labels may not contain information that otherwise would be required under the FD&C Act.

The Moderna COVID-19 Vaccine (2024-2025 Formula) is authorized for emergency use with the following product-specific information required to be made available to vaccination providers and recipients, respectively (referred to as "authorized labeling"[38]):

> Fact Sheet for Healthcare Providers Administering Vaccine: Emergency Use Authorization of Moderna COVID-19 Vaccine (2024-2025 Formula), For Individuals 6 Months Through 11 Years of Age
>
> Fact Sheet for Recipients and Caregivers About Moderna COVID-19 Vaccine (2024-2025 Formula) Which Has Emergency Use Authorization (EUA) to Prevent Coronavirus Disease 2019 (COVID-19) in Individuals 6 Months Through 11 Years of Age

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of Moderna COVID-19 Vaccine (2024-2025 Formula)[39] and Moderna COVID-19 Vaccine (2023-2024 Formula), when used to prevent COVID-19 and used in accordance with this Scope of Authorization (Section II), outweigh their known and potential risks.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that Moderna COVID-19 Vaccine (2024-2025 Formula) and Moderna COVID-19 Vaccine (2023-2024 Formula) may be effective in preventing COVID-19 when used in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act.

Having reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, I have concluded that Moderna COVID-19 Vaccine (2024-2025 Formula) and Moderna COVID-19 Vaccine (2023-2024 Formula) (as described in this Scope of Authorization (Section II)) meet the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of Moderna COVID-19 Vaccine (2024-2025 Formula) and Moderna COVID-19 Vaccine (2023-2024 Formula) under this EUA must be consistent with, and may not

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[38] This authorized labeling required to be made available to vaccination providers and recipients also contains information about uses of SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) that are authorized under this EUA.

[39] The conclusions supporting authorization stated in this section (Section II) also apply to SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) when used under this authorization.

exceed, the terms of the Authorization, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section III). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), Moderna COVID-19 Vaccine (2024-2025 Formula) and Moderna COVID-19 Vaccine (2023-2024 Formula) are authorized to prevent COVID-19 as described in the Scope of Authorization (Section II) under this EUA, despite the fact that they do not meet certain requirements otherwise required by applicable federal law.

III. Conditions of Authorization

Pursuant to Section 564 of the Act, I am establishing the following conditions on this authorization:

ModernaTX, Inc. and Authorized Distributor(s)

A. ModernaTX, Inc. and authorized distributor(s) will ensure that the authorized labeling (i.e., Fact Sheets) will be made available to vaccination providers, recipients, and caregivers consistent with the terms of this letter.

B. ModernaTX, Inc. and authorized distributor(s) will ensure that appropriate storage and cold chain is maintained until delivered to healthcare facilities or other vaccine receipt sites.

C. ModernaTX, Inc. will ensure that the terms of this EUA are made available to all relevant stakeholders (e.g., authorized distributors and vaccination providers) involved in distributing or receiving authorized Moderna COVID-19 Vaccine(2024-2025 Formula). ModernaTX, Inc. will provide to all relevant stakeholders a copy of this letter of authorization and communicate any subsequent amendments that might be made to this letter of authorization and its authorized labeling.

D. ModernaTX, Inc. may develop and disseminate instructional and educational materials (e.g., video regarding vaccine handling, storage/cold-chain management, preparation, disposal) that are consistent with the authorized emergency use of the Moderna COVID-19 Vaccine (2024-2025 Formula) as described in the letter of authorization and authorized labeling, without FDA's review and concurrence, when necessary to meet public health needs during an emergency. Any instructional and educational materials that are inconsistent with the authorized labeling are prohibited.

E. ModernaTX, Inc. may request changes to this authorization, including to the authorized Fact Sheets. Any request for changes to this EUA must be submitted to Office of Vaccines Research and Review (OVRR)/Center for Biologics Evaluation

and Research (CBER). Such changes require appropriate authorization prior to implementation.[40]

F. ModernaTX, Inc. will report to Vaccine Adverse Event Reporting System (VAERS):
- Serious adverse events (irrespective of attribution to vaccination);
- Cases of myocarditis;
- Cases of pericarditis;
- Cases of Multisystem Inflammatory Syndrome; and
- Cases of COVID-19 that result in hospitalization or death, that are reported to ModernaTX, Inc.

These reports should be submitted to VAERS as soon as possible but no later than 15 calendar days from initial receipt of the information by ModernaTX, Inc.

G. ModernaTX, Inc. must submit to Investigational New Drug application (IND) number 19745 periodic safety reports monthly, or at another appropriate reporting interval determined by the Office of Biostatistics and Pharmacovigilance (OBPV)/CBER, in accordance with a due date agreed upon with OBPV/CBER beginning after the first full calendar month after authorization. Each periodic safety report is required to contain descriptive information which includes:
- A narrative summary and analysis of adverse events submitted during the reporting interval, including interval and cumulative counts by age groups, special populations (e.g., pregnant women), and adverse events of special interest;
- A narrative summary and analysis of vaccine administration errors, whether or not associated with an adverse event, that were identified since the last reporting interval;
- Newly identified safety concerns in the interval;
- Actions taken since the last report because of adverse experiences (for example, changes made to Healthcare Providers Administering Vaccine (Vaccination Providers) Fact Sheet, changes made to studies or studies initiated); and

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[40] The following types of revisions may be authorized without reissuing this letter: (1) changes to the authorized labeling; (2) non-substantive editorial corrections to this letter; (3) new types of authorized labeling, including new fact sheets; (4) new carton/container labels; (5) expiration dating extensions; (6) changes to manufacturing processes, including tests or other authorized components of manufacturing; (7) new conditions of authorization to require data collection or study. All changes to the authorization require review and concurrence from OVRR. For changes to the authorization, including the authorized labeling, of the type listed in (3), (6), or (7), review and concurrence is required from the Preparedness and Response Team (PREP)/Office of the Center Director (OD)/CBER and the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS).

- Cumulative doses distributed, and doses distributed during the reporting interval, for Moderna COVID-19 Vaccine (2024-2025 Formula).

H. No changes will be implemented to the description of the product, manufacturing process, facilities, or equipment without notification to and concurrence by FDA.

I. All manufacturing facilities will comply with Current Good Manufacturing Practice requirements.

J. ModernaTX, Inc. will submit to the EUA file Certificates of Analysis (CoA) for each drug product lot at least 48 hours prior to vaccine distribution. The CoA will include the established specifications and specific results for each quality control test performed on the final drug product lot.

K. ModernaTX, Inc. will submit to the EUA file quarterly manufacturing reports, starting in July 2021, that include a listing of all Drug Substance and Drug Product lots produced after issuance of this authorization. This report must include lot number, manufacturing site, date of manufacture, and lot disposition, including those lots that were quarantined for investigation or those lots that were rejected. Information on the reasons for lot quarantine or rejection must be included in the report.

L. ModernaTX, Inc. and authorized distributor(s) will maintain records regarding release of Moderna COVID-19 Vaccine (2024-2025 Formula) and Moderna COVID-19 Vaccine (2023-2024 Formula), for distribution (i.e., lot numbers, quantity, release date).

M. ModernaTX, Inc. and authorized distributor(s) will make available to FDA upon request any records maintained in connection with this EUA.

N. ModernaTX, Inc. will conduct post-authorization observational studies to evaluate the association between Moderna COVID-19 Vaccine (Original monovalent), Moderna COVID-19 Vaccine, Bivalent, Moderna COVID-19 Vaccine (2023-2024 Formula), and Moderna COVID-19 Vaccine (2024-2025 Formula), and a pre-specified list of adverse events of special interest, including myocarditis and pericarditis, along with deaths and hospitalizations, and severe COVID-19. The study population should include individuals administered the Moderna COVID-19 Vaccine (Original monovalent) (previously, but no longer authorized for use in the U.S.) as a primary series (6 months of age and older) or booster dose (18 years of age and older); individuals administered a dose of the Moderna COVID-19 Vaccine, Bivalent (previously, but no longer authorized for use in the U.S.) (6 months of age and older); Moderna COVID-19 Vaccine (2023-2024 Formula) (6 months through 11 years of age) (previously, but no longer authorized for use in the U.S); and Moderna COVID-19 Vaccine (2024-2025 Formula) (6 months through 11 years of age) under this EUA in the general U.S. population, and populations of interest such

as healthcare workers, pregnant women, immunocompromised individuals, subpopulations with specific comorbidities. The studies should be conducted in large scale databases with an active comparator. ModernaTX, Inc. will provide protocols and status update reports to the IND 19745 with agreed-upon study designs and milestone dates.

O. ModernaTX, Inc., working with its contract research organization, will continue to monitor the performance of its clinical investigators in ongoing clinical studies of its vaccines and will report to FDA promptly any significant deviations from the protocols.

Vaccination Providers

P. Vaccination providers will administer the vaccines in accordance withthis authorization.

Q. Vaccination providers will provide the Fact Sheet for Recipients and Caregivers to each individual receiving vaccination and provide the necessary information for receiving their dose(s).

R. Vaccination providers administering the vaccines must report the following information associated with the administration of the vaccines of which they become aware to VAERS in accordance with the Fact Sheet for Healthcare Providers Administering Vaccine:
   - Vaccine administration errors whether or not associated with an adverse event
   - Serious adverse events (irrespective of attribution to vaccination)
   - Cases of myocarditis
   - Cases of pericarditis
   - Cases of Multisystem Inflammatory Syndrome
   - Cases of COVID-19 that result in hospitalization or death

   Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html. Vaccination providers submitting VAERS reports should specify the date of birth for the vaccine recipient and the vaccine formula (e.g., "Moderna COVID-19 Vaccine (2024-2025 Formula) EUA") in the VAERS report. More information is available at vaers.hhs.gov or by calling 1-800-822-7967. To the extent feasible, report to ModernaTX, Inc., by contacting 1-866-663-3762, by providing a copy of the VAERS form to ModernaTX, Inc., Fax: 1-866-599-1342 or by email; ModernaPV@modernatx.com.

S. Vaccination providers will conduct any follow-up requested by the U.S. government, including CDC, FDA, or other designee, regarding adverse events to the extent feasible given the emergency circumstances.

T. Vaccination providers will ensure that any records associated with this EUA are maintained until notified by FDA. Such records will be made available to CDC and FDA for inspection upon request.

U. Vaccination providers receiving authorized Moderna COVID-19 Vaccine (2024-2025 Formula) will ensure that appropriate storage and cold chain is maintained.

Conditions Related to Printed Matter, Advertising, and Promotion

V. All descriptive printed matter, advertising, and promotional material relating to the use of the Moderna COVID-19 Vaccine (2024-2025 Formula) shall be consistent with the authorized labeling, as well as the terms set forth in this EUA, and meet the requirements set forth in Section 502(a) and (n), as applicable, of the FD&C Act and FDA implementing regulations. In addition, such materials shall:

- Be tailored to the intended audience.
- Present the same risk information relating to the major side effects and contraindications concurrently in the audio and visual parts of the presentation for advertising and promotional materials in audio-visual format.
- Be accompanied by the authorized labeling, if the promotional materials are not subject to Section 502(n) of the Act.

ModernaTX, Inc. must submit such materials to FDA accompanied by Form FDA-2253 by the time of initial dissemination or first use.

W. All descriptive printed matter, advertising, and promotional material relating to the use of the Moderna COVID-19 Vaccine (2024-2025 Formula) clearly and conspicuously shall state that:

- The Moderna COVID-19 Vaccine (2024-2025 Formula) has not been approved or licensed by FDA, but has been authorized for emergency use by FDA, under an EUA to prevent Coronavirus Disease 2019 (COVID-19) for use in individuals 6 months through 11 years of age; and
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of the medical product under Section 564(b)(1) of the FD&C Act unless the declaration is terminated or authorization revoked sooner.

If the Agency notifies ModernaTX , Inc. that any descriptive printed matter, advertising, or promotional materials do not meet the terms set forth in Conditions V and W of this EUA, ModernaTX, Inc. must cease distribution of such descriptive printed matter, advertising, or promotional materials in accordance with the Agency's notification. Furthermore, as part of its notification, the Agency may also require ModernaTX, Inc. to issue corrective communication(s).

Condition Related to Export

X. If the Moderna COVID-19 Vaccine (2024-2025 Formula), is exported from the United States, conditions C, D, and P through W do not apply, but export is permitted only if 1) the regulatory authorities of the country in which the vaccine will be used are fully informed that this vaccine is subject to an EUA and is not approved or licensed by FDA and 2) the intended use of the vaccine will comply in all respects with the laws of the country in which the product will be used. The requirement in this letter that the authorized labeling (i.e., Fact Sheets) be made available to vaccination providers, recipients, and caregivers in condition A will not apply if the authorized labeling (i.e., Fact Sheets) are made available to the regulatory authorities of the country in which the vaccine will be used.

If the Moderna COVID-19 Vaccine (2023-2024 Formula), is exported from the United States, conditions C, D, and P through W do not apply, but export is permitted only if 1) the vaccine was manufactured on or before August 22, 2024, 2) the regulatory authorities of the country in which the vaccine will be used are fully informed that this vaccine is subject to an EUA and is not approved or licensed by FDA, 3) the intended use of the vaccine will comply in all respects with the laws of the country in which the product will be used, 4) the Fact Sheets that were authorized as of September 11, 2023 (Fact Sheet for Recipients and Caregivers) and as of November 1, 2023 (Fact Sheet for Healthcare Providers Administering Vaccine) are made available, upon request, to the regulatory authorities of the countries in which the vaccine will be used, and 5) the regulatory authorities are informed that the Moderna COVID-19 Vaccine (2023-2024 Formula) and associated Fact Sheets are no longer authorized for use in the United States and that FDA is not currently revising the Fact Sheets with updated information.

Condition with Respect to Use of Licensed Product

Y. This authorization also covers the use of the licensed SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) product in certain immunocompromised individuals turning from 11 to 12 years of age during the vaccination series, as described in Scope of Authorization (Section II) under this EUA. Conditions A through V in this letter apply when SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) is provided for the uses described in this subsection III.Y, except that 1) product manufactured and labeled in accordance with the approved BLA is deemed to satisfy the manufacturing, labeling, and distribution requirements of this authorization; and 2) product lots that are released in accordance with the approved BLA are deemed to satisfy the requirement of this authorization for submission of CoAs to the EUA 48 hours prior to lot distribution.

IV. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

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Peter Marks, M.D., Ph.D.
Director
Center for Biologics Evaluation and Research

EXHIBIT B

Fact Sheet for Healthcare Providers Administering Vaccine

(Starts on Following Page)

Individuals using assistive technology may not be able to fully access the information contained in this file. For assistance, please call 800-835-4709 or 240-402-8010, extension 1. CBER Consumer Affairs Branch or send an e-mail to: ocod@fda.hhs.gov and include 508 Accommodation and the title of the document in the subject line of your e-mail.

FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE: EMERGENCY USE AUTHORIZATION OF MODERNA COVID-19 VACCINE (2024-2025 FORMULA), FOR INDIVIDUALS 6 MONTHS THROUGH 11 YEARS OF AGE

HIGHLIGHTS OF EMERGENCY USE AUTHORIZATION (EUA)
These highlights of the EUA do not include all the information needed to use Moderna COVID-19 Vaccine under the EUA. See the FULL FACT SHEET FOR HEALTHCARE PROVIDERS for Moderna COVID-19 Vaccine.

Moderna COVID-19 Vaccine
Injectable suspension, for intramuscular use
2024-2025 Formula
Original EUA Authorized Date: 12/2020
Most Recent EUA Authorized Date: 8/2024

----------RECENT MAJOR CHANGES----------
Dosage and Administration,
Preparation for Administration (2.1) 8/2024

----------EMERGENCY USE AUTHORIZATION----------
The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for the emergency use of Moderna COVID-19 Vaccine (2024-2025 Formula) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 6 months through 11 years of age.

See Full Fact Sheet for Healthcare Providers for the justification for emergency use of Moderna COVID-19 Vaccine (2024-2025 Formula), information on available alternatives, and additional information on COVID-19.

----------DOSAGE AND ADMINISTRATION----------
For intramuscular use. (2)

Individuals 6 Months Through 4 Years of Age by Moderna COVID-19 Vaccination Status (2.3)

Number of Previous Doses of Moderna COVID-19 Vaccine(s)[a]	Moderna COVID-19 Vaccine (2024-2025 Formula) Dosing Regimen, Dose and Schedule[b]
0[c]	2 doses,[d] 0.25 mL each Dose 1: month 0 Dose 2: month 1
1	Single Dose, 0.25 mL One month after receipt of a previous dose of Moderna COVID-19 vaccine[a]
≥2	Single dose, 0.25 mL ≥2 months after receipt of the last previous dose of Moderna COVID-19 vaccine[a]

[a] Previous dose refers to a dose of any prior Moderna COVID-19 Vaccine that is no longer authorized for use in the United States.
[b] For individuals with certain kinds of immunocompromise previously vaccinated with a Moderna COVID-19 vaccine, see text following the tables for dosing information.
[c] Not previously vaccinated with any COVID-19 vaccine.
[d] Individuals turning from 4 years to 5 years of age during the vaccination series should receive both doses with Moderna COVID-19 Vaccine (2024-2025 Formula).

Individuals 5 Years Through 11 Years of Age Irrespective of COVID-19 Vaccination Status (2.3)

Moderna COVID-19 Vaccine (2024-2025 Formula) Dosing Regimen, Dose and Schedule[a]
Single dose, 0.25 mL (If previously vaccinated, administer the dose ≥2 months after receipt of the last previous dose of COVID-19 vaccine[b])

[a] For individuals with certain kinds of immunocompromise, see text below tables for further dosing information.
[b] Previous dose refers to a dose of any prior COVID-19 vaccine that is no longer authorized for use in the United States.

Individuals with Certain Kinds of Immunocompromise

Individuals with certain kinds of immunocompromise 6 months through 11 years of age should complete at least a three-dose series with a COVID-19 vaccine, each dose one month apart. At least 1 dose should be with a COVID-19 vaccine (2024-2025 Formula). Certain kinds of immunocompromise refers to individuals who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
Moderna COVID-19 Vaccine is an injectable suspension.

A single dose is 0.25 mL. (3)

----------CONTRAINDICATIONS----------
Do not administer Moderna COVID-19 Vaccine to individuals with a known history of a severe allergic reaction (e.g., anaphylaxis) to any component of Moderna COVID-19 Vaccine or to individuals who had a severe allergic reaction (e.g., anaphylaxis) following a previous dose of a Moderna COVID-19 vaccine. (4)

----------WARNINGS AND PRECAUTIONS----------
Postmarketing data with authorized or approved mRNA COVID-19 vaccines demonstrate increased risks of myocarditis and pericarditis, particularly within the first week following vaccination. For Moderna COVID-19 Vaccine, the observed risk is highest in males 18 years through 24 years of age. (5.2)

----------ADVERSE REACTIONS----------
Solicited adverse reactions included:
- **6 months through 36 months of age:** Injection site erythema, pain and swelling; axillary (or groin) swelling/tenderness, fever, irritability/crying, loss of appetite and sleepiness.
- **37 months through 11 years of age:** Injection site erythema, pain and swelling; arthralgia, axillary (or groin) swelling/tenderness, chills, fatigue, fever, headache, myalgia and nausea/vomiting. (6.1)

Vaccination providers must report all vaccine administration errors, all serious adverse events, cases of myocarditis, cases of pericarditis, cases of Multisystem Inflammatory Syndrome (MIS), and cases of COVID-19 that result in hospitalization or death following administration of Moderna COVID-19 Vaccine (2024-2025 Formula) to the Vaccine Adverse Event Reporting System (VAERS) by submitting online at https://vaers.hhs.gov/reportevent.html. For further assistance with reporting to VAERS call 1-800-822-7967. To the extent feasible, report adverse events to ModernaTX, Inc. at 1-866-

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* Sections or subsections omitted from the EUA are not listed

FULL FACT SHEET FOR HEALTHCARE PROVIDERS

1 EMERGENCY USE AUTHORIZATION

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for the emergency use of Moderna COVID-19 Vaccine (2024-2025 Formula) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 6 months through 11 years of age.

Justification for Emergency Use of Vaccines During the COVID-19 Pandemic

There is currently an outbreak of COVID-19 caused by SARS-CoV-2. The Secretary of the Department of Health and Human Services (HHS) has:

- Determined that there is a public health emergency, or a significant potential for a public health emergency related to COVID-19.[1]
- Declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic.[2]

An EUA is an FDA authorization for the emergency use of an unapproved product or unapproved use of an approved product (i.e., drug, biological product, or device) in the United States under certain circumstances including, but not limited to, when the Secretary of HHS declares that the use of EUA authority is justified, based on a determination that there is a public health emergency, or a significant potential for a public health emergency, that affects or has a significant potential to affect, national security or the health and security of United States citizens living abroad, and that involves biological agent(s) or a disease or condition that may be attributable to such agent(s). Criteria for issuing an EUA include:

- The biological agent(s) can cause a serious or life-threatening disease or condition;
- Based on the totality of the available scientific evidence (including data from adequate and well-controlled clinical trials, if available), it is reasonable to believe that:

[1] *See* U.S. Department of Health and Human Services, Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3. February 4, 2020; https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency. *See also* U.S. Department of Health and Human Services, Amended Determination of a Public Health Emergency or Significant Potential for a Public Health Emergency Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b). March 15, 2023 ("Amended Determination"); https://www.federalregister.gov/documents/2023/03/20/2023-05609/covid-19-emergency-use-authorization-declaration.

[2] *See* U.S. Department of Health and Human Services, Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3, 85 FR 18250 (April 1, 2020); https://www.federalregister.gov/documents/2020/04/01/2020-06905/emergency-use-authorization-declaration. *See also* Amended Determination ("The declarations issued pursuant to section 564(b)(1) of the FD&C Act that circumstances exist justifying the authorization of emergency use of certain in vitro diagnostics, personal respiratory protective devices, other medical devices and drugs and biological products, as set forth in those declarations, and that are based on the February 4, 2020 determination, remain in effect until those declarations are terminated in accordance with section 564 of the FD&C Act.").

    - The product may be effective in diagnosing, treating, or preventing the serious or life-threatening disease or condition;
    - The known and potential benefits of the product – when used to diagnose, prevent, or treat such disease or condition – outweigh the known and potential risks of the product, taking into consideration the material threat posed by the biological agent(s); and
- There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the serious or life-threatening disease or condition.

Information Regarding Available Alternative Vaccines for the Prevention of COVID-19 in Individuals 6 Months Through 11 Years of Age

There may be clinical trials or availability under EUA of other COVID-19 vaccines, including vaccines that contain or encode the spike protein of the Omicron variant KP.2 of SARS-CoV-2.

For information on clinical studies of Moderna COVID-19 Vaccine and other vaccines for the prevention of COVID-19, see www.clinicaltrials.gov.

2 DOSAGE AND ADMINISTRATION

For intramuscular use.

2.1 Preparation for Administration

- Thaw before use following the instructions below.

	Thaw in Refrigerator Between 2°C to 8°C (36°F to 46°F)	**Thaw at Room Temperature Between 15°C to 25°C (59°F to 77°F)**
Single Dose Pre-Filled Syringe	One syringe: Thaw for 1 hour.	One syringe: Thaw for 45 minutes.
	Carton of 10 syringes: Thaw for 2 hours and 30 minutes.	Carton of 10 syringes: Thaw for 2 hours and 15 minutes.

- After thawing, do not refreeze.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
- Moderna COVID-19 Vaccine is a white to off-white suspension. It may contain white or translucent product-related particulates. Do not administer if vaccine is discolored or contains other particulate matter.
- **Do not shake.** Discard after single use.
    - With tip cap upright, remove tip cap by twisting counterclockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
    - Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.

2.2 Administration

Administer the 0.25 mL dose of Moderna COVID-19 Vaccine intramuscularly.

2.3 Dose and Schedule

Individuals 6 Months Through 4 Years of Age by Moderna COVID-19 Vaccination Status

Number of Previous Doses of Moderna COVID-19 Vaccine(s)[a]	Moderna COVID-19 Vaccine (2024-2025 Formula) Dosing Regimen, Dose and Schedule[b]
0[c]	2 doses,[d] 0.25 mL each Dose 1: month 0 Dose 2: month 1
1	Single Dose, 0.25 mL One month after receipt of a previous dose of Moderna COVID-19 vaccine[a]
≥2	Single dose, 0.25 mL ≥2 months after receipt of the last previous dose of Moderna COVID-19 vaccine[a]

[a] Previous dose refers to a dose of any prior Moderna COVID-19 Vaccine that is no longer authorized for use in the United States.
[b] For individuals with certain kinds of immunocompromise previously vaccinated with a Moderna COVID-19 vaccine, see text following the tables for dosing information.
[c] Not previously vaccinated with any COVID-19 vaccine.
[d] Individuals turning from 4 years to 5 years of age during the vaccination series should receive both doses with Moderna COVID-19 Vaccine (2024-2025 Formula).

Individuals 5 Years Through 11 Years of Age Irrespective of COVID-19 Vaccination Status

Moderna COVID-19 Vaccine (2024-2025 Formula) Dosing Regimen, Dose and Schedule[a]
Single dose, 0.25 mL (If previously vaccinated, administer the dose ≥2 months after receipt of the last previous dose of COVID-19 vaccine[b])

[a] For individuals with certain kinds of immunocompromise, see text following tables for dosing information.
[b] Previous dose refers to a dose of any prior COVID-19 vaccine that is no longer authorized for use in the United States.

Individuals 6 Months through 11 Years of Age with Certain Kinds of Immunocompromise

Individuals 6 months through 11 years of age with certain kinds of immunocompromise[3] should complete at least a three-dose series with a COVID-19 vaccine, each dose one month apart.[4] At least 1 dose should be with a COVID-19 vaccine (2024-2025 Formula).

- If previously not vaccinated, complete the three-dose series with Moderna COVID-19 Vaccine (2024-2025 Formula).
- If previously vaccinated with one or two dose(s) of any prior formula of Moderna COVID-19 Vaccine,[5] complete the remaining dose(s) in the three-dose series with Moderna COVID-19 Vaccine (2024-2025 Formula).
- If previously vaccinated with three or more doses of any prior formula of COVID-19 vaccines,[5] administer a single dose of Moderna COVID-19 Vaccine (2024-2025 Formula) at least two months following the last dose.

An additional dose of Moderna COVID-19 Vaccine (2024-2025 Formula) may be administered at least 2 months following the last dose of a COVID-19 vaccine (2024-2025 Formula).[6,7] Additional doses of Moderna COVID-19 Vaccine (2024-2025 Formula) may be administered at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances. The timing of the additional doses may be based on the individual's clinical circumstances.

3 DOSAGE FORMS AND STRENGTHS

Moderna COVID-19 Vaccine is an injectable suspension.

A single dose is 0.25 mL.

[3] Certain kinds of immunocompromise refers to individuals who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.
[4] COVID-19 vaccine, each dose of the three-doses series given one month apart, refers to Moderna COVID-19 vaccines. For individuals with certain kinds of immunocompromise turning from 11 years to 12 years of age during the vaccination series, complete the 3-dose series with 1 or 2 doses, as applicable, of SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) on or after the date the individual turns 12 years of age. If the individual turning 12 years of age receives two doses of SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) to complete the vaccination series or receives a dose of SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) less than 2 months after receipt of the last previous dose of COVID-19 vaccine to complete the vaccination series, then those uses of SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) are authorized under EUA. The FDA has authorized under EUA these uses of SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula), which is an FDA-licensed vaccine indicated for active immunization to prevent COVID-19 in individuals 12 years of age and older. Refer to www.spikevax.com/pi for additional information about SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula).
[5] These prior COVID-19 vaccines are no longer authorized for use in the U.S.
[6] For immunocompromised individuals 6 months through 4 years of age, the last dose of a COVID-19 vaccine (2024-2025 Formula) refers to a dose with Moderna COVID-19 Vaccine (2024-2025 Formula).
[7] For immunocompromised individuals 5 years through 11 years of age, the last dose of a COVID-19 vaccine (2024-2025 Formula) refers to a dose with Pfizer-BioNTech COVID-19 Vaccine (2024-2025 Formula) or Moderna COVID-19 Vaccine (2024-2025 Formula).

4 CONTRAINDICATIONS

Do not administer Moderna COVID-19 Vaccine to individuals with a history of a severe allergic reaction (e.g., anaphylaxis) to any component of Moderna COVID-19 Vaccine *[see Description (11)]* or to individuals who had a severe allergic reaction (e.g., anaphylaxis) following a previous dose of a Moderna COVID-19 vaccine.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment must be immediately available to manage potential anaphylactic reactions following administration of Moderna COVID-19 Vaccine.

Monitor Moderna COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention (CDC) guidelines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html).

5.2 Myocarditis and Pericarditis

Postmarketing data with authorized or approved mRNA COVID-19 vaccines demonstrate increased risks of myocarditis and pericarditis, particularly within the first week following vaccination. For Moderna COVID-19 Vaccine, the observed risk is highest in males 18 years through 24 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae.

The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressive therapy, may have a diminished response to Moderna COVID-19 Vaccine.

5.5 Limitations of Vaccine Effectiveness

Moderna COVID-19 Vaccine may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In clinical studies contributing to the safety assessment of Moderna COVID-19 Vaccine (2024-2025 Formula), participants received a 2-dose series one month apart (referred to as primary series) and subsequent doses referred to as booster doses, as described in Table 1 below.

Table 1: Clinical Studies

Study	Age	Dosing Regimen	Vaccine Recipients
Study 1 (NCT04470427)	18 years of age and older	Primary Series: 2 doses (100 mcg mRNA per dose) of Moderna COVID-19 Vaccine (Original Monovalent)[a] 1 month apart	15,184
Study 2 (NCT04405076)	18 years of age and older	First Booster Dose: Single dose (50 mcg mRNA) of Moderna COVID-19 Vaccine (Original Monovalent)	171
Study 3 (NCT04649151)	12 years through 17 years of age	Primary Series: 2 doses (100 mcg mRNA per dose) of Moderna COVID-19 Vaccine (Original Monovalent) 1 month apart	2,486
		First Booster Dose: Single dose (50 mcg mRNA) of Moderna COVID-19 Vaccine (Original Monovalent)	1,405
Study 4 (NCT04796896)	6 years through 11 years of age	Primary Series: 2 doses (50 mcg mRNA per dose) of Moderna COVID-19 Vaccine (Original Monovalent) 1 month apart	3,007
		First Booster Dose: Single dose (25 mcg mRNA) of Moderna COVID-19 Vaccine (Original Monovalent)	1,294
	6 months through 5 years of age	Primary Series: 2 doses (25 mcg mRNA per dose) of Moderna COVID-19 Vaccine (Original Monovalent) 1 month apart	4,792
		First Booster Dose: Single dose (10 mcg mRNA) of Moderna COVID-19 Vaccine (Original Monovalent)	145
Study 5 (NCT04927065)	18 years of age and older	Second Booster Dose: Single dose (50 mcg mRNA) of bivalent vaccine (Original and Omicron BA.1)[b]	437

[a] Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu 1 strain (Original)
[b] Vaccine encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu 1 strain (Original) and Omicron variant lineage BA.1 (Omicron BA.1), not authorized or approved in the U.S.

The safety data accrued with the Moderna COVID-19 Vaccine (Original monovalent, no longer authorized for use in the U.S.), Moderna's bivalent COVID-19 vaccine (Original and Omicron BA.1) [not authorized or approved in the U.S., hereafter referred to as bivalent vaccine (Original and Omicron BA.1)] and Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) (no longer authorized for use in the U.S.) are relevant to Moderna COVID-19 Vaccine (2024-2025 Formula) because these vaccines are manufactured using the same process.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates

observed in the clinical trials of a vaccine cannot be directly compared with rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

Moderna COVID-19 Vaccine (Original Monovalent) Administered as a Two-Dose Primary Series

Participants 18 Years of Age and Older

The safety of Moderna COVID-19 Vaccine was evaluated in a Phase 3 clinical trial with multiple parts. The randomized, placebo-controlled, observer-blind phase of the trial was conducted in the United States involving 30,346 participants 18 years of age and older who received at least one dose of Moderna COVID-19 Vaccine (100 mcg mRNA; n=15,184) or placebo (n=15,162) (Study 1, NCT04470427). Upon issuance of the Emergency Use Authorization (December 18, 2020) for Moderna COVID-19 Vaccine, participants were unblinded in a phased manner over a period of months to offer placebo participants Moderna COVID-19 Vaccine. The median duration of follow-up for safety after the second injection during the blinded phase was 4 months. The median duration of follow up for safety after the second injection including both the blinded phase and the open-label phase was 6 months.

In Study 1, the median age of the population was 52 years (range 18-95); 75.2% of participants were 18 years through 64 years of age and 24.8% were 65 years of age and older. Overall, 52.6% of the participants were male, 47.4% were female, 20.5% were Hispanic or Latino, 79.2% were White, 10.2% were African American, 4.6% were Asian, 0.8% were American Indian or Alaska Native, 0.2% were Native Hawaiian or Pacific Islander, 2.0% were other races, and 2.1% were Multiracial. Demographic characteristics were similar between participants who received Moderna COVID-19 Vaccine and those who received placebo.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for 28 days following each dose. Serious adverse events and medically attended adverse events will be recorded for the entire study duration (2 years). Among the 30,346 participants who had received at least 1 dose of vaccine (N=15,184) or placebo (N=15,162), unsolicited adverse events that occurred within 28 days following any vaccination were reported by 31.3% of participants (n=4,752) who received Moderna COVID-19 Vaccine and 28.6% of participants (n=4,338) who received placebo.

During the 28-day follow-up period following any dose, lymphadenopathy-related events were reported by 1.7% of vaccine recipients and 0.8% of placebo recipients. These events included lymphadenopathy, lymphadenitis, lymph node pain, vaccination-site lymphadenopathy, injection-site lymphadenopathy, and axillary mass. This imbalance is consistent with the imbalance observed for solicited axillary swelling/tenderness at the injected arm.

During the 7-day follow-up period of any vaccination, hypersensitivity events of injection site rash or injection site urticaria, likely related to vaccination, were reported by 6 participants in the Moderna COVID-19 Vaccine group and none in the placebo group. Delayed injection site reactions that began >7 days after vaccination were reported in 1.4% of vaccine recipients and

0.7% of placebo recipients. Delayed injection site reactions included pain, erythema, and swelling and are likely related to vaccination.

In the blinded portion of the study, there were 8 reports of facial paralysis (including Bell's palsy) in the Moderna COVID-19 Vaccine group, and 3 in the placebo group. In the 28-day follow-up period there were two cases of facial paralysis in the Moderna COVID-19 Vaccine group, which occurred on 8 and 22 days, respectively, after vaccination, and one in the placebo group, which occurred 17 days after vaccination. Currently available information on facial paralysis is insufficient to determine a causal relationship with the vaccine.

In the blinded portion of the study, there were 50 reports of herpes zoster in the Moderna COVID-19 Vaccine group, and 23 in the placebo group. In the 28-day period after any vaccination, there were 22 cases of herpes zoster in the Moderna COVID-19 Vaccine group, and 15 in the placebo group. Currently available information on herpes zoster infection is insufficient to determine a causal relationship with the vaccine.

There were no other notable patterns or numerical imbalances between treatment groups for specific categories of adverse events (including other neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to Moderna COVID-19 Vaccine.

Serious Adverse Events

During the blinded phase of the study, serious adverse events were reported by 1.8% (n=268) of participants who received Moderna COVID-19 Vaccine and 1.9% (n=292) of participants who received placebo.

There were three serious adverse events of angioedema/facial swelling in the vaccine group in recipients with a history of injection of dermatological fillers. The onset of swelling was reported 1-2 days after the second dose and was likely related to vaccination.

There were no other notable patterns or imbalances between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to Moderna COVID-19 Vaccine.

Participants 12 Years Through 17 Years of Age

The safety of Moderna COVID-19 Vaccine was evaluated in an ongoing Phase 3 clinical trial with multiple parts. The randomized, placebo-controlled, observer-blind clinical trial was conducted in the United States involving 3,726 participants 12 years through 17 years of age who received at least one dose of Moderna COVID-19 Vaccine (100 mcg mRNA; n=2,486) or placebo (n=1,240) (Study 3, NCT04649151). Participants started to enter an open-label, observational phase after May 10, 2021. After October 1, 2021, cases of potential myocarditis and/or pericarditis that were identified by the investigator or Applicant were adjudicated by an independent Cardiac Event Adjudication Committee (CEAC) to determine if they met the CDC definition of confirmed or probable myocarditis and/or pericarditis. A safety analysis was conducted in participants who received Moderna COVID-19 Vaccine (n=2,486) with a cut-off

date of January 31, 2022. In these analyses, the median duration of follow-up including both the blinded and open-label phases was 312 days after Dose 2 and 95.7% of study participants had at least 6 months of follow-up after Dose 2.

Overall, 51.4% were male, 48.6% were female, 11.6% were Hispanic or Latino, 83.8% were White, 3.4% were African American, 6.0% were Asian, 0.5% were American Indian or Alaska Native, <0.1% were Native Hawaiian or Pacific Islander, 1.0% were other races, and 4.5% were Multiracial. Demographic characteristics were similar among participants who received Moderna COVID-19 Vaccine and those who received placebo.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for 28 days following each dose. Serious adverse events and medically attended adverse events were recorded for the entire study duration. Among the 3,726 participants who had received at least 1 dose of vaccine (n=2,486) or placebo (n=1,240), unsolicited adverse events that occurred within 28 days following any vaccination were reported by 23.4% of participants (n=582) who received Moderna COVID-19 Vaccine and 19.1% of participants (n=237) who received placebo.

In the open-label portion of the study, a 14-year-old male experienced probable myocarditis with onset of symptoms 1 day after Dose 2 of Moderna COVID-19 Vaccine. Symptoms resolved after 8 days and no sequelae were observed at 5 months. This event was considered related to Moderna COVID-19 Vaccine and was subsequently adjudicated by the CEAC as probable myocarditis. There were no cases of myocarditis among placebo recipients.

During the 28-day follow-up period following any dose, lymphadenopathy-related events were reported by 6.0% of vaccine recipients and 0.6% of placebo recipients. These events included lymphadenopathy, vaccination-site lymphadenopathy, and injection-site lymphadenopathy which were plausibly related to vaccination. This imbalance is consistent with the imbalance observed for solicited axillary swelling/tenderness in the injected arm.

During the 28-day follow-up period following any dose, hypersensitivity events of injection site rash or injection site urticaria, likely related to vaccination, were reported by 0.3% of participants in the Moderna COVID-19 Vaccine group and <0.1% in the placebo group. Delayed injection site reactions that began >7 days after vaccination were reported in 1.5% of vaccine recipients and in <0.1% of placebo recipients. Delayed injection site reactions included pain, erythema, and swelling and are likely related to vaccination.

There were no other notable patterns or numerical imbalances between treatment groups for specific categories of adverse events (including other neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to Moderna COVID-19 Vaccine.

Serious Adverse Events

During the blinded portion of the study, serious adverse events were reported by 0.4% (n=9) of participants who received Moderna COVID-19 Vaccine and 0.2% (n=3) of participants who

received placebo. In the open-label phase, an additional 12 Moderna COVID-19 Vaccine recipients reported serious adverse events. There were no serious adverse events considered causally related to the vaccine.

There were no notable patterns or imbalances between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to Moderna COVID-19 Vaccine.

Participants 6 Years Through 11 Years of Age

Study 4 (NCT04796896) is a Phase 2/3 clinical trial with multiple parts. The study included a randomized, placebo-controlled, observer-blind clinical trial component conducted in the United States and Canada. Safety data for Moderna COVID-19 Vaccine from the blinded portion of Study 3 included data in 4,002 participants 6 years through 11 years of age who received at least one dose of Moderna COVID-19 Vaccine (50 mcg mRNA; n=3,007) or placebo (n=995). As of the data cutoff date of November 10, 2021, the median duration of blinded follow-up for safety was 51 days after Dose 2, and 1,284 participants had been followed for at least 2 months after Dose 2 (vaccine=1,006, placebo=218).

Demographic characteristics in Study 4 were similar among participants who received Moderna COVID-19 Vaccine and those who received placebo. Overall, 50.8% were male, 49.2% were female, 18.5% were Hispanic or Latino, 65.6% were White, 10.0% were African American, 9.9% were Asian, 0.4% were American Indian or Alaska Native, <0.1% were Native Hawaiian or Pacific Islander, 2.1% were other races, and 10.6% were Multiracial.

Solicited Adverse Reactions

Local and systemic adverse reactions and use of antipyretic medication were solicited in an electronic diary for 7 days following each injection (i.e., day of vaccination and the next 6 days) among participants receiving Moderna COVID-19 Vaccine (n=3,006) and participants receiving placebo (n=994) with at least 1 documented dose. Events that persisted for more than 7 days were followed until resolution.

The reported number and percentage of the solicited local and systemic adverse reactions in participants 6 years through 11 years of age by dose in Study 4 are presented in Table 2.

Table 2: Number and Percentage of Participants With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After Each Dose in Participants 6 Years Through 11 Years (Solicited Safety Set, Dose 1 and Dose 2)†

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=3,004) n (%)	**Dose 2** (N=2,988) n (%)	**Dose 1** (N=993) n (%)	**Dose 2** (N=969) n (%)
Local Adverse Reactions				
Pain	2,796 (93.1)	2,832 (94.8)	465 (46.8)	480 (49.5)
Pain, Grade 3[b]	28 (0.9)	81 (2.7)	0 (0)	2 (0.2)
Axillary swelling/tenderness	465 (15.5)	537 (18.0)	84 (8.5)	65 (6.7)
Axillary swelling/tenderness, Grade 3[b]	3 (<0.1)	3 (0.1)	1 (0.1)	2 (0.2)
Swelling (hardness) ≥25 mm	354 (11.8)	507 (17.0)	12 (1.2)	12 (1.2)
Swelling (hardness), Grade 3: >100 mm	19 (0.6)	20 (0.7)	1 (0.1)	0 (0)
Erythema (redness) ≥25 mm	349 (11.6)	559 (18.7)	13 (1.3)	10 (1.0)
Erythema (redness), Grade 3: >100 mm	16 (0.5)	33 (1.1)	1 (0.1)	1 (0.1)
Systemic Adverse Reactions				
Fatigue	1,298 (43.2)	1,925 (64.5)	334 (33.6)	335 (34.6)
Fatigue, Grade 3[c]	31 (1.0)	191 (6.4)	8 (0.8)	8 (0.8)
Headache	938 (31.2)	1,622 (54.3)	306 (30.8)	275 (28.4)
Headache, Grade 3[c]	18 (0.6)	119 (4.0)	4 (0.4)	8 (0.8)
Myalgia	438 (14.6)	843 (28.2)	96 (9.7)	105 (10.8)
Myalgia, Grade 3[c]	11 (0.4)	71 (2.4)	1 (0.1)	1 (0.1)
Arthralgia	260 (8.7)	482 (16.1)	75 (7.6)	84 (8.7)
Arthralgia, Grade 3[c]	3 (<0.1)	25 (0.8)	1 (0.1)	0 (0)
Chills	309 (10.3)	904 (30.3)	67 (6.7)	74 (7.6)
Chills, Grade 3[d]	3 (<0.1)	19 (0.6)	0 (0)	0 (0)
Nausea/vomiting	325 (10.8)	716 (24.0)	107 (10.8)	97 (10.0)
Nausea/vomiting, Grade 3[b]	5 (0.2)	19 (0.6)	0 (0)	0 (0)

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=3,004) n (%)	**Dose 2** (N=2,988) n (%)	**Dose 1** (N=993) n (%)	**Dose 2** (N=969) n (%)
Fever ≥38.0°C / >100.4°F	99 (3.3)	714 (23.9)	15 (1.5)	19 (2.0)
Fever, Grade 3: 39.0° - 40.0°C / 102.1° - 104.0°F	17 (0.6)	115 (3.8)	2 (0.2)	2 (0.2)
Use of antipyretic or pain medication	730 (24.3)	1,423 (47.6)	95 (9.6)	93 (9.6)

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).
† No Grade 4 adverse reactions were reported.
[a] Placebo was a saline solution.
[b] Grade 3 pain, axillary swelling/tenderness, nausea/vomiting: Defined as prevents daily activity.
[c] Grade 3 fatigue, headache, myalgia, arthralgia: Defined as significant; prevents daily activity.
[d] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.

Solicited local and systemic adverse reactions reported following administration of Moderna COVID-19 Vaccine had a median duration of 2 to 3 days.

An assessment of reactogenicity among participants with evidence of prior SARS-CoV-2 infection (immunologic or virologic evidence of prior SARS-CoV-2 infection [defined as positive RT-PCR test and/or positive Elecsys immunoassay result at Day 1]) compared to those with no evidence of infection at baseline (negative RT-PCR test and negative Elecsys immunoassay result at Day 1) was conducted. In ages 6 years through 11 years, 8.6% of participants (vaccine=257, placebo=87) had evidence of prior SARS-CoV-2 infection at baseline. Table 3 presents the number and percentage of the solicited local and systemic adverse reactions in Moderna COVID-19 Vaccine participants starting within 7 days after each dose by SARS-CoV-2 status.

Table 3: Number and Percentage of Participants 6 Years Through 11 Years Who Received Vaccine With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After Each Dose by SARS-CoV-2 Status (Solicited Safety Set, Dose 1 and Dose 2)†

	Baseline SARS-CoV-2 Positive		Baseline SARS-CoV-2 Negative	
	Dose 1 (N=257) n (%)	**Dose 2** (N= 255) n (%)	**Dose 1** (N=2,700) n (%)	**Dose 2** (N=2,686) n (%)
Local Adverse Reactions				
Pain	234 (91.1)	240 (94.1)	2,522 (93.4)	2,547 (94.8)
Pain, Grade 3[a]	3 (1.2)	8 (3.1)	23 (0.9)	72 (2.7)
Axillary swelling/tenderness	63 (24.5)	48 (18.8)	394 (14.6)	474 (17.6)

	Baseline SARS-CoV-2 Positive		Baseline SARS-CoV-2 Negative	
	Dose 1 (N=257) n (%)	**Dose 2** (N= 255) n (%)	**Dose 1** (N=2,700) n (%)	**Dose 2** (N=2,686) n (%)
Axillary swelling/tenderness, Grade 3[a]	1 (0.4)	0 (0)	2 (<0.1)	3 (0.1)
Swelling (hardness) ≥25 mm	29 (11.3)	29 (11.4)	317 (11.7)	468 (17.4)
Swelling (hardness), Grade 3: >100 mm	1 (0.4)	2 (0.8)	17 (0.6)	18 (0.7)
Erythema (redness) ≥25 mm	26 (10.1)	34 (13.3)	317 (11.7)	518 (19.3)
Erythema (redness), Grade 3: >100 mm	0 (0)	1 (0.4)	15 (0.6)	32 (1.2)
Systemic Adverse Reactions				
Fatigue	129 (50.2)	145 (56.9)	1,145 (42.4)	1,744 (65.0)
Fatigue, Grade 3[b]	11 (4.3)	14 (5.5)	20 (0.7)	169 (6.3)
Headache	127 (49.4)	134 (52.5)	796 (29.5)	1,458 (54.3)
Headache, Grade 3[b]	8 (3.1)	11 (4.3)	10 (0.4)	103 (3.8)
Myalgia	63 (24.5)	75 (29.4)	367 (13.6)	747 (27.8)
Myalgia, Grade 3[b]	2 (0.8)	3 (1.2)	9 (0.3)	63 (2.3)
Arthralgia	33 (12.8)	43 (16.9)	224 (8.3)	427 (15.9)
Arthralgia, Grade 3[b]	0 (0)	1 (0.4)	3 (0.1)	22 (0.8)
Chills	51 (19.8)	68 (26.7)	251 (9.3)	815 (30.4)
Chills, Grade 3[c]	1 (0.4)	1 (0.4)	2 (<0.1)	17 (0.6)
Nausea/vomiting	36 (14.0)	54 (21.2)	281 (10.4)	646 (24.1)
Nausea/vomiting, Grade 3[a]	1 (0.4)	0 (0)	4 (0.1)	18 (0.7)
Fever ≥38.0°C / >100.4°F	42 (16.3)	61 (23.9)	55 (2.0)	635 (23.6)
Fever, Grade 3: 39.0° - 40.0°C / 102.1° - 104.0°F	5 (1.9)	6 (2.4)	12 (0.4)	108 (4.0)

* 7 days included day of vaccination and the subsequent 6 days. Events were collected in the electronic diary (e-diary).

† No Grade 4 adverse reactions were reported.

[a] Grade 3 pain, axillary swelling/tenderness, nausea/vomiting: Defined as prevents daily activity.

[b] Grade 3 fatigue, headache, myalgia, arthralgia: Defined as significant; prevents daily activity.

[c] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for up to 28 days following each dose. Serious adverse events and medically attended adverse events will be recorded for the entire study duration. As of November 10, 2021, among participants who had received at least 1 dose of vaccine or placebo (vaccine=3,007, placebo=995), unsolicited adverse events that occurred within 28 days following each vaccination were reported by 29.6% of participants (n=891) who received Moderna COVID-19 Vaccine and 25.1% of participants (n=250) who received placebo. In these analyses, 98.6% of study participants had at least 28 days of follow-up after Dose 2.

During the 28-day follow-up period following any dose, lymphadenopathy-related events were reported by 1.8% of vaccine recipients and 0.6% of placebo recipients. These events included lymphadenopathy, lymph node pain, injection-site lymphadenopathy, and vaccination-site lymphadenopathy which were plausibly related to vaccination. This imbalance is consistent with the imbalance observed for solicited axillary swelling/tenderness in the injected arm.

During the 28-day follow-up period following any dose, hypersensitivity adverse events were reported in 4.3% of vaccine recipients and 2.1% of placebo recipients. Hypersensitivity events in the vaccine group included injection site rash and injection site urticaria, which are likely related to vaccination. Delayed injection site reactions that began >7 days after vaccination were reported in 2.7% of vaccine recipients and in 0.2% of placebo recipients. Delayed injection site reactions included pain, erythema, and swelling and are likely related to vaccination.

During the 28-day follow-up period following any dose, events of abdominal pain (including abdominal pain, abdominal pain upper, and abdominal pain lower) were reported by 1.1% of vaccine recipients and 0.6% of placebo recipients. Currently available information is insufficient to determine a causal relationship with the vaccine.

There were no other notable patterns or numerical imbalances between treatment groups for specific categories of adverse events that would suggest a causal relationship to Moderna COVID-19 Vaccine.

Serious Adverse Events

As of November 10, 2021, serious adverse events were reported by 0.2% (n=6) of participants who received Moderna COVID-19 Vaccine and 0.2% (n=2) participants who received placebo. None of the events in the Moderna COVID-19 Vaccine group were considered related to vaccine. In these analyses, 98.6% of study participants had at least 28 days of follow-up after Dose 2, and the median follow-up time for all participants was 51 days after Dose 2.

There were no notable patterns or imbalances between treatment groups for specific categories of serious adverse events that would suggest a causal relationship to Moderna COVID-19 Vaccine.

Additional Safety Analyses

Participants 6 years through 11 years in Study 4 started to enter an open-label, observational phase after November 1, 2021. A long-term safety analysis was conducted in participants 6 years through 11 years from Study 4 who received Moderna COVID-19 Vaccine (n=3,007) with a cut-off date of February 21, 2022. In these analyses, the median duration of follow-up including both the blinded and open-label phases was 158 days after Dose 2. Through the cut-off date, there were no serious adverse events causally related to the vaccine.

Participants 6 Months Through 5 Years of Age

Study 4 (NCT04796896) is a Phase 2/3 clinical trial with multiple parts. The study included a randomized, placebo-controlled, observer-blind clinical trial component conducted in the United States and Canada. Safety data for Moderna COVID-19 Vaccine from the blinded portion of Study 4 included data in 6,388 participants 6 months through 5 years of age who received at least one dose of Moderna COVID-19 Vaccine (25 mcg mRNA; n=4,792) or placebo (n=1,596). As of the data cutoff date of February 21, 2022, the median duration of blinded follow-up for safety for participants 6 months through 23 months was 68 days after Dose 2. For participants 2 years through 5 years, the median duration of blinded follow-up for safety was 71 days after Dose 2.

For participants 6 months through 23 months, 51.1% were male, 48.9% were female, 13.2% were Hispanic or Latino, 79.0% were White, 3.1% were African American, 4.9% were Asian, 0.2% were American Indian or Alaska Native, 0.0% were Native Hawaiian or Pacific Islander, 1.5% were other races, and 10.6% were Multiracial. For participants 2 years through 5 years, 50.8% were male, 49.2% were female, 14.2% were Hispanic or Latino, 76.5% were White, 4.5% were African American, 6.0% were Asian, 0.4% were American Indian or Alaska Native, 0.3% were Native Hawaiian or Pacific Islander, 1.5% were other races, and 10.4% were Multiracial. Demographic characteristics were similar among participants who received Moderna COVID-19 Vaccine and those who received placebo.

Solicited Adverse Reactions

Local and systemic adverse reactions and use of antipyretic medication were solicited in an electronic diary for 7 days following each injection (i.e., day of vaccination and the next 6 days) among participants receiving Moderna COVID-19 Vaccine and participants receiving placebo with at least 1 documented dose (for participants 6 through 23 months, vaccine=1,758, placebo=585; for participants 24 months to 36 months, vaccine=986, placebo=338; for participants 37 months to 5 years, vaccine=2,030, placebo=659). Events that persisted for more than 7 days were followed until resolution.

The reported number and percentage of the solicited local and systemic adverse reactions by dose in Study 4 participants 6 months through 23 months of age are presented in Table 4, participants 24 months through 36 months of age are presented in Table 5, and participants 37 months to 5 years are presented in Table 6.

Table 4: Number and Percentage of Participants With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After Each Dose in Participants 6 Months Through 23 Months (Solicited Safety Set, Dose 1 and Dose 2)†

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N= 1,746) n (%)	**Dose 2** (N=1,596) n (%)	**Dose 1** (N= 582) n (%)	**Dose 2** (N=526) n (%)
Local Adverse Reactions				
Pain	652 (37.4)	738 (46.2)	175 (30.1)	135 (25.7)
Axillary (or groin) swelling/tenderness	102 (5.9)	148 (9.3)	26 (4.5)	28 (5.3)
Erythema (redness) ≥5 mm	150 (8.6)	216 (13.5)	24 (4.1)	20 (3.8)
Erythema (redness) Grade 3: >50 mm	5 (0.3)	14 (0.9)	2 (0.3)	0 (0)
Swelling (hardness) ≥5 mm	146 (8.4)	244 (15.3)	15 (2.6)	11 (2.1)
Swelling (hardness) Grade 3: >50 mm	5 (0.3)	14 (0.9)	0 (0)	0 (0)
Systemic Adverse Reactions				
Irritability/crying	1,175 (67.6)	1,021 (64.3)	361 (62.1)	307 (58.5)
Irritability/crying, Grade 3[b]	24 (1.4)	25 (1.6)	6 (1.0)	5 (1.0)
Sleepiness	645 (37.1)	558 (35.1)	217 (37.3)	175 (33.3)
Sleepiness, Grade 3[c]	4 (0.2)	1 (<0.1)	1 (0.2)	1 (0.2)
Loss of appetite	524 (30.2)	510 (32.1)	152 (26.2)	132 (25.1)
Loss of appetite, Grade 3[d]	10 (0.6)	16 (1.0)	1 (0.2)	2 (0.4)
Fever >38.0°C / >100.4°F	191 (11.0)	232 (14.6)	49 (8.4)	44 (8.4)
Fever, Grade 3: 39.6° - 40.0°C / 103.2° - 104.0°F	11 (0.6)	7 (0.4)	3 (0.5)	6 (1.1)
Fever, Grade 4: >40.0°C / >104.0°F	1 (<0.1)	3 (0.2)	1 (0.2)	0 (0)
Use of antipyretic or pain medication	482 (27.6)	543 (34.0)	141 (24.2)	111 (21.1)

N=Included 16 individuals aged 2 years to 4 years randomized in the 6 months through 23 months of age group stratum (13 in the Moderna COVID-19 Vaccine group and 3 in the placebo group).

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).

† Absence of rows for Grade 3 or Grade 4 adverse reactions indicates no events were reported.

[a] Placebo was a saline solution.

[b] Grade 3 irritability/crying: Defined as lasting >3 hours or inconsolable.
[c] Grade 3 sleepiness: Defined as sleeps most of the time, hard to arouse.
[d] Grade 3 loss of appetite: Defined as missed >2 feeds/meals completely or refuses most feeds/meals.

Table 5: Number and Percentage of Participants With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After Each Dose in Participants 24 Months Through 36 Months (Solicited Safety Set, Dose 1 and Dose 2)†

	Moderna COVID-19 Vaccine		**Placebo[a]**	
	Dose 1 (N=944) n (%)	**Dose 2** (N=963) n (%)	**Dose 1** (N=320) n (%)	**Dose 2** (N=330) n (%)
Local Adverse Reactions				
Pain	500 (53.1)	654 (67.9)	119 (37.2)	146 (44.2)
Pain, Grade 3[b]	3 (0.3)	5 (0.5)	0 (0)	0 (0)
Axillary (or groin) swelling/tenderness	49 (5.2)	84 (8.7)	18 (5.6)	15 (4.5)
Axillary (or groin) swelling/tenderness, Grade 3[b]	0 (0)	1 (0.1)	0 (0)	0 (0)
Erythema (redness) ≥5 mm	94 (10.0)	117 (12.1)	13 (4.1)	10 (3.0)
Erythema (redness), Grade 3: >50 mm	6 (0.6)	9 (0.9)	2 (0.6)	0 (0)
Swelling (hardness) ≥5 mm	77 (8.2)	111 (11.5)	11 (3.4)	7 (2.1)
Swelling (hardness), Grade 3: >50 mm	5 (0.5)	8 (0.8)	2 (0.6)	0 (0)
Systemic Adverse Reactions				
Irritability/crying	513 (54.5)	523 (54.3)	163 (51.1)	148 (44.8)
Irritability/crying, Grade 3[c]	12 (1.3)	10 (1.0)	6 (1.9)	2 (0.6)
Sleepiness	285 (30.3)	347 (36.0)	92 (28.8)	89 (27.0)
Sleepiness, Grade 3[d]	2 (0.2)	1 (0.1)	0 (0)	0 (0)
Loss of appetite	225 (23.9)	294 (30.5)	71 (22.3)	69 (20.9)
Loss of appetite, Grade 3[e]	7 (0.7)	8 (0.8)	1 (0.3)	0 (0)
Fever ≥38.0°C / >100.4°F	106 (11.3)	182 (18.9)	25 (7.8)	35 (10.6)
Fever, Grade 3: 39.6° - 40.0°C / 103.2° - 104.0°F	3 (0.3)	12 (1.2)	3 (0.9)	0 (0)
Fever, Grade 4: >40.0°C / >104.0°F	3 (0.3)	3 (0.3)	1 (0.3)	0 (0)

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=944) n (%)	**Dose 2** (N=963) n (%)	**Dose 1** (N=320) n (%)	**Dose 2** (N=330) n (%)
Use of antipyretic or pain medication	193 (20.4)	292 (30.3)	59 (18.4)	62 (18.8)

N=Included 36 individuals younger than 2 years of age randomized in the 2 years through 5 years of age group stratum (24 in the Moderna COVID-19 Vaccine group and 12 in the placebo group). All of these 36 individuals had eDiary for 6 months to ≤36 months age group.

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).

† Absence of rows for Grade 3 or Grade 4 adverse reactions indicates no events were reported.

[a] Placebo was a saline solution.

[b] Grade 3 pain, axillary swelling/tenderness: Defined as prevents daily activity.

[c] Grade 3 irritability/crying: Defined as lasting >3 hours or inconsolable.

[d] Grade 3 sleepiness: Defined as sleeps most of the time, hard to arouse.

[e] Grade 3 loss of appetite: Defined as missed >2 feeds/meals completely or refuses most feeds/meals.

Table 6: Number and Percentage of Participants With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After Each Dose in Participants 37 Months Through 5 Years (Solicited Safety Set, Dose 1 and Dose 2)†

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=2,013) n (%)	**Dose 2** (N= 1,975) n (%)	**Dose 1** (N=650) n (%)	**Dose 2** (N= 629) n (%)
Local Adverse Reactions				
Pain	1,313 (65.2)	1,445 (73.2)	263 (40.5)	249 (39.6)
Pain, Grade 3[b]	1 (<0.1)	6 (0.3)	0 (0)	0 (0)
Axillary (or groin) swelling/tenderness	156 (7.7)	183 (9.3)	38 (5.8)	16 (2.5)
Erythema (redness) ≥25 mm	70 (3.5)	143 (7.2)	1 (0.2)	5 (0.8)
Erythema (redness), Grade 3: >100 mm	6 (0.3)	3 (0.2)	1 (0.2)	0 (0)
Swelling (hardness) ≥25 mm	57 (2.8)	129 (6.5)	6 (0.9)	4 (0.6)
Swelling (hardness), Grade 3: >100 mm	5 (0.2)	5 (0.3)	0 (0)	0 (0)
Systemic Adverse Reactions				
Fatigue	807 (40.1)	956 (48.4)	236 (36.3)	185 (29.4)
Fatigue, Grade 3[c]	21 (1.0)	45 (2.3)	11 (1.7)	8 (1.3)
Headache	232 (11.5)	310 (15.7)	78 (12.0)	51 (8.1)

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=2,013) n (%)	**Dose 2** (N= 1,975) n (%)	**Dose 1** (N=650) n (%)	**Dose 2** (N= 629) n (%)
Headache, Grade 3[c]	5 (0.2)	8 (0.4)	2 (0.3)	1 (0.2)
Fever ≥38.0°C / >100.4°F	155 (7.7)	316 (16.0)	33 (5.1)	28 (4.5)
Fever, Grade 3: 39.0° - 40.0°C / 102.1° - 104.0°F	23 (1.1)	58 (2.9)	4 (0.6)	2 (0.3)
Fever, Grade 4: >40.0°C / >104.0°F	0 (0)	2 (0.1)	1 (0.2)	0 (0)
Myalgia	200 (9.9)	310 (15.7)	60 (9.2)	47 (7.5)
Myalgia, Grade 3[c]	5 (0.2)	9 (0.5)	2 (0.3)	3 (0.5)
Chills	129 (6.4)	245 (12.4)	40 (6.2)	31 (4.9)
Chills, Grade 3[c]	1 (<0.1)	4 (0.2)	0 (0)	2 (0.3)
Nausea/vomiting	137 (6.8)	194 (9.8)	50 (7.7)	30 (4.8)
Nausea/vomiting, Grade 3[c]	7 (0.3)	6 (0.3)	2 (0.3)	0 (0)
Arthralgia	124 (6.2)	168 (8.5)	32 (4.9)	28 (4.5)
Arthralgia, Grade 3[c]	2 (<0.1)	3 (0.2)	1 (0.2)	0 (0)
Use of antipyretic or pain medication	305 (15.2)	508 (25.7)	62 (9.5)	43 (6.8)

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).
† Absence of rows for Grade 3 or Grade 4 adverse reactions indicates no events were reported.
[a] Placebo was a saline solution.
[b] Grade 3 pain: Defined as prevents daily activity.
[c] Grade 3 fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting: Defined as prevents daily activity.

Solicited local and systemic adverse reactions reported following administration of Moderna COVID-19 Vaccine had a median duration of 2 to 3 days for participants 6 months through 23 months of age and 2 days for participants 2 years through 5 years of age.

Solicited Adverse Reactions Among Participants with Evidence of Prior SARS-CoV-2 Infection

An assessment of reactogenicity among participants with evidence of prior SARS-CoV-2 infection (immunologic or virologic evidence of prior SARS-CoV-2 infection [defined as positive RT-PCR test and/or positive Elecsys immunoassay result at Day 1]) compared to those with no evidence of infection at baseline (negative RT-PCR test and negative Elecsys immunoassay result at Day 1) was conducted. In the 6 months through 23 months of age cohort, 6.1% of participants (vaccine=106, placebo=38) had evidence of prior SARS-CoV-2 infection at

baseline. In the 2 years through 5 years of age cohort, 8.6% of participants (vaccine=266, placebo=82) had evidence of prior SARS-CoV-2 infection at baseline. In each age cohort, fever (temperature >38°C) was reported in a greater proportion of baseline SARS-CoV-2 positive vaccine participants compared to baseline SARS-CoV-2 negative vaccine participants. There were no notable differences in other reactogenicity events.

Safety of a 25-mcg dose in children 6 months through 4 years of age previously vaccinated with 2 or more doses of a Moderna COVID-19 vaccine is supported by these data on solicited adverse reactions in participants with evidence of prior SARS-CoV-2 infection, since the second dose represents a third exposure to the SARS-CoV-2 Spike antigen.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for up to 28 days following each dose and follow-up is ongoing. Serious adverse events and medically attended adverse events will be recorded for the entire study duration.

As of February 21, 2022, among participants 6 months through 23 months of age who had received at least 1 dose of vaccine or placebo (vaccine=1,761, placebo=589), unsolicited adverse events that occurred within 28 days following each vaccination were reported by 49.3% of participants (n=869) who received Moderna COVID-19 Vaccine and 48.2% of participants (n=284) who received placebo. In these analyses, 83.1% of study participants 6 months through 23 months of age had at least 28 days of follow-up after Dose 2. Among participants 2 years through 5 years of age who had received at least 1 dose of vaccine or placebo (vaccine=3,031, placebo=1,007), unsolicited adverse events that occurred within 28 days following each vaccination were reported by 40.0% of participants (n=1,212) who received Moderna COVID-19 Vaccine and 37.5% of participants (n=378) who received placebo. In these analyses, 89.3% of study participants 2 years through 5 years of age had at least 28 days of follow-up after Dose 2.

During the 28-day follow-up period following any dose, lymphadenopathy-related events were reported by 1.5% of vaccine recipients and 0.2% of placebo recipients who were 6 months through 23 months of age and 0.9% of vaccine recipients and <0.1% of placebo recipients who were 2 years through 5 years of age. These events included lymphadenopathy, injection-site lymphadenopathy, and vaccination-site lymphadenopathy which were plausibly related to vaccination. This imbalance is consistent with the imbalance observed for solicited axillary (or groin) swelling/tenderness in the injected limb.

During the 28-day follow-up period following any dose, hypersensitivity adverse events were reported in 3.9% of vaccine recipients and 5.3% of placebo recipients who were 6 months through 23 months of age and 3.5% of vaccine recipients and 2.5% of placebo recipients who were 2 years through 5 years of age. Hypersensitivity events in the vaccine group included injection site rash and injection site urticaria, which are likely related to vaccination. Delayed injection site reactions that began >7 days after vaccination were reported in 1.2% of vaccine recipients and no placebo recipients who were 6 months through 23 months of age and 1.4% of vaccine recipients and <0.1% of placebo recipients who were 2 years through 5 years of age.

Delayed injection site reactions included pain, erythema, and swelling and are likely related to vaccination.

During the 28-day follow-up period following any dose, events of abdominal pain (including abdominal pain, abdominal pain upper, and abdominal discomfort) were reported by 0.7% of vaccine recipients and 0.4% of placebo recipients who were 2 years through 5 years of age. Currently available information is insufficient to determine a causal relationship with the vaccine.

There were no other notable patterns or numerical imbalances between treatment groups for specific categories of adverse events that would suggest a causal relationship to Moderna COVID-19 Vaccine.

Serious Adverse Events

As of February 21, 2022, serious adverse events were reported by 0.9% (n=15) of participants who received vaccine and 0.2% (n=1) of participants who received placebo who were 6 months through 23 months of age and 0.3% (n=9) of participants who received Moderna COVID-19 Vaccine and 0.2% (n=2) of participants who received placebo who were 2 years through 5 years of age. In these analyses, 83.1% of study participants 6 months through 23 months of age had at least 28 days of follow-up after Dose 2, and the median follow-up time for all participants was 68 days after Dose 2. In these analyses, 89.3% of study participants 2 years through 5 years of age had at least 28 days of follow-up after Dose 2, and the median follow-up time for all participants was 71 days after Dose 2.

In participants 6 months through 23 months of age who received the vaccine, a 1-year-old female experienced serious adverse events of a Grade 3 fever 6 hours after Dose 1 and a febrile convulsion 1 day after Dose 1. These events were considered related to vaccination. In participants 2 years through 5 years of age who received Moderna COVID-19 Vaccine, none of the events were considered related to vaccine.

Moderna COVID-19 Vaccine (Original Monovalent) Administered as a First Booster Dose Following a Primary Series of Moderna COVID-19 Vaccine (Original Monovalent)

Participants 18 Years of Age and Older

Study 2 was a Phase 2, randomized, observer-blind, placebo-controlled, dose-confirmation study to evaluate the safety, reactogenicity, and immunogenicity of Moderna COVID-19 Vaccine in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses 1 month apart of Moderna COVID-19 Vaccine primary series (100 mcg mRNA per dose). In an open-label-phase of the study, 171 of those participants received a single booster dose (50 mcg mRNA) at least 6 months (range of 5.8 to 8.5 months) after receiving the second dose of the primary series.

Among the 171 booster dose recipients, the median age was 55 years (range 18-87); 77.8% of participants were 18 years through 64 years of age, 22.2% were 65 years of age and older, 39.2%

were male, 60.8% were female, 5.8% were Hispanic or Latino, 95.9% were White, 2.9% were African American, 0.6% were Asian, and 0.6% were American Indian or Alaska Native.

Unsolicited Adverse Events

Overall, the 171 participants who received a booster dose had a median follow-up time of 176 days after the booster dose to the database lock date (November 23, 2021). Through 28 days after the booster dose, unsolicited adverse events were reported by 14.6% of participants (n=25) after the booster dose. There were no unsolicited adverse events not already captured by solicited local and systemic reactions that were considered causally related to Moderna COVID-19 Vaccine.

Serious Adverse Events

There were no serious adverse events reported from the booster dose through 28 days after the booster dose. Through the database lock date (November 23, 2021), there were no serious adverse events following the booster dose considered causally related to Moderna COVID-19 Vaccine.

Participants 12 Years Through 17 Years of Age

Safety data for a booster dose of Moderna COVID-19 Vaccine in adolescents were collected in an ongoing Phase 3 clinical trial with multiple parts. The open-label booster portion of the study included 1,405 participants who were 12 years through 17 years of age at the time of first dose of the primary series and who received a booster dose of Moderna COVID-19 Vaccine (50 mcg mRNA) at least 5 months (range 2.1 to 16.9 months) after the second dose of the primary series (Study 3, NCT04649151). Overall, 51.5% were male, 48.5% were female, 13.4% were Hispanic or Latino, 84.9% were White, 3.1% were African American, 4.9% were Asian, 0.5% were American Indian or Alaska Native, <0.1% were Native Hawaiian or Pacific Islander, 0.7% were other races, and 5.2% were Multiracial. The median duration of follow-up for safety after the booster dose was 204 days.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for up to 28 days following the booster dose. Serious adverse events and medically attended adverse events were recorded for the entire study duration. As of August 15, 2022, among the 1,405 participants who had received a booster dose of Moderna COVID-19 Vaccine, unsolicited adverse events that occurred within 28 days following vaccination were reported by 14.9% of participants (n=209). In these analyses, 85.7% of study participants had at least 6 months of follow-up after the booster dose. Overall, there were no notable differences in the safety profiles observed between participants who had received a booster dose of Moderna COVID-19 Vaccine and those who had received a primary series.

Serious Adverse Events

Through the cut-off date of August 15, 2022, with a median follow-up duration of 204 days after the booster dose, there were no serious adverse events considered causally related to the vaccine.

Participants 6 Years Through 11 Years of Age

Safety data for a booster dose of Moderna COVID-19 Vaccine in individuals 6 years through 11 years of age were collected in an ongoing Phase 2/3 clinical trial with multiple parts. The open-label booster portion of the study involved 1,294 participants 6 years through 11 years of age who received a booster dose of Moderna COVID-19 Vaccine (25 mcg mRNA) at least 6 months after the second dose of the primary series (Study 4, NCT04796896). Overall, 51.9% were male, 48.1% were female, 15.6% were Hispanic or Latino, 65.7% were White, 11.0% were African American, 7.8% were Asian, 0.5% were American Indian or Alaska Native, <0.1% were Native Hawaiian or Pacific Islander, 1.9% were other races, and 11.8% were Multiracial. As of the data cutoff date of May 23, 2022, the median duration of follow-up for safety was 29 days after the booster dose.

Solicited Adverse Reactions

Local and systemic adverse reactions and use of antipyretic medication were solicited in an electronic diary for 7 days following the injection (i.e., day of vaccination and the next 6 days) among participants receiving Moderna COVID-19 Vaccine. Events that persisted for more than 7 days were followed until resolution.

Table 7 presents the frequency and severity of reported solicited local and systemic adverse reactions among Study 4 Moderna COVID-19 Vaccine booster dose recipients 6 years through 11 years of age within 7 days of a booster vaccination.

Table 7: Number and Percentage of Participants 6 Years Through 11 Years of Age With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After the Moderna COVID-19 Vaccine Booster Dose (Solicited Safety Set)†

	Moderna COVID-19 Vaccine Booster Dose (N=1,280) n (%)
Local Adverse Reactions	
Pain	1,152 (90.1)
Pain, Grade 3[a]	24 (1.9)
Axillary swelling/tenderness	355 (27.8)
Axillary swelling/tenderness, Grade 3[a]	4 (0.3)
Swelling (hardness) ≥25 mm	139 (10.9)
Swelling (hardness), Grade 3: >100 mm	4 (0.3)
Erythema (redness) ≥25 mm	137 (10.7)
Erythema (redness), Grade 3: >100 mm	4 (0.3)
Systemic Adverse Reactions	
Fatigue	625 (48.9)
Fatigue, Grade 3[b]	47 (3.7)

	Moderna COVID-19 Vaccine Booster Dose (N=1,280) n (%)
Headache	489 (38.2)
Headache, Grade 3[b]	22 (1.7)
Myalgia	269 (21.0)
Myalgia, Grade 3[b]	19 (1.5)
Arthralgia	160 (12.5)
Arthralgia, Grade 3[b]	12 (0.9)
Chills	179 (14.0)
Chills, Grade 3[c]	4 (0.3)
Nausea/vomiting	168 (13.1)
Nausea/vomiting, Grade 3[a]	6 (0.5)
Fever ≥38.0°C / >100.4°F	108 (8.5)
Fever, Grade 3: 39.0° - 40.0°C / 102.1° - 104.0°F	16 (1.3)
Fever, Grade 4: >40° C / >104.0°F	1 (<0.1)
Use of antipyretic or pain medication	462 (36.1)

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).
† Absence of rows for Grade 4 adverse reactions indicates no events were reported.
[a] Grade 3 pain, axillary swelling/tenderness, nausea/vomiting: Defined as prevents daily activity.
[b] Grade 3 fatigue, headache, myalgia, arthralgia: Defined as significant; prevents daily activity.
[c] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.

In participants who received a booster dose, the median duration of solicited local and systemic adverse reactions was 3 days.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for up to 28 days following the booster dose. Serious adverse events and medically attended adverse events will be recorded for the entire study duration. As of May 23, 2022, among the 1,294 participants who had received a booster dose, unsolicited adverse events that occurred within 28 days following vaccination were reported by 13.1% of participants (n=169). In these analyses, 55.4% of study participants had at least 28 days of follow-up after the booster dose. Serum sickness-like reaction with onset 10 days following administration of a booster dose was reported in an 8-year-old participant. This event was assessed as related to vaccination. After initiation of treatment with antihistamines and steroids, symptoms resolved within 15 days with the exception of intermittent urticaria that was ongoing 31 days after the onset of the reaction.

Serious Adverse Events

As of May 23, 2022, with a median follow-up duration of 29 days after the booster dose, there was one serious adverse event of abdominal pain reported 16 days following the booster dose by a 7-year-old participant. Currently available information is insufficient to determine a causal relationship with the vaccine.

Participants 17 Months Through 5 Years of Age

Safety data in support of a booster dose of Moderna COVID-19 Vaccine in individuals 6 months through 5 years of age were collected in participants 17 months through 5 years of age at the time of the booster dose in an ongoing Phase 2/3 clinical trial with multiple parts. The open-label booster portion of the study involved 145 participants 17 months through 5 years of age who received a booster dose of Moderna COVID-19 Vaccine (10 mcg mRNA) at least 6 months (range 8-13 months; median 10 months) after the completion of the Moderna COVID-19 Vaccine two-dose primary series (Study 4, NCT04796896). Overall, 55.2% were male, 44.8% were female, 10.3% were Hispanic or Latino, 80.0% were White, 2.8% were African American, 6.2% were Asian, 0.7% were American Indian or Alaska Native, 0.0% were Native Hawaiian or Pacific Islander, 2.8% were other races, and 7.6% were Multiracial. As of the data cutoff date of August 18, 2022, the median duration of follow-up for safety after the booster dose was 99 days.

Solicited Adverse Reactions

Local and systemic adverse reactions and use of antipyretic medication were solicited in an electronic diary for 7 days following the injection (i.e., day of vaccination and the next 6 days) among participants receiving Moderna COVID-19 Vaccine (10 mcg mRNA). Events that persisted for more than 7 days were followed until resolution.

The frequency and severity of reported solicited local and systemic adverse reactions within 7 days of a booster vaccination among participants 17 months through 36 months are presented in Table 8, and among participants 37 months through 5 years are presented in Table 9.

Table 8: Number and Percentage of Participants 17 Months Through 36 Months of Age With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After the Moderna COVID-19 Vaccine Booster Dose (Solicited Safety Set)†

	Moderna COVID-19 Vaccine Booster Dose (N=120[a]) n (%)
Local Adverse Reactions	
Pain	50 (41.7)
Erythema (redness) ≥5 mm	13 (10.8)
Erythema (redness) Grade 3: >50 mm	1 (0.8)
Swelling (hardness) ≥5 mm	13 (10.8)
Axillary (or groin) swelling/tenderness	5 (4.2)
Systemic Adverse Reactions	
Irritability/crying	63 (52.5)
Sleepiness	32 (26.7)
Loss of appetite	28 (23.3)
Fever >38.0°C / >100.4°F	12 (10.1)
Fever, Grade 3: 39.6° - 40.0°C / 103.2° - 104.0°F	2 (1.7)
Fever, Grade 4: >40.0°C / >104.0°F	1 (0.8)
Use of antipyretic or pain medication	24 (20.0)

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).
† Absence of rows for Grade 3 or Grade 4 adverse reactions indicates no events were reported.
[a] Four participants were older than 36 months of age at the time of the booster dose; however, solicited adverse reactions were collected and graded using the diary card and grading scale for participants 6 months through 36 months of age.

Table 9: Number and Percentage of Participants 37 Months Through 5 Years With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After the Moderna COVID-19 Vaccine Booster Dose (Solicited Safety Set)†

	Moderna COVID-19 Vaccine Booster Dose (N=25) n (%)
Local Adverse Reactions	
Pain	14 (56.0)
Swelling (hardness) ≥25 mm	3 (12.0)
Axillary (or groin) swelling/tenderness	1 (4.0)
Erythema (redness) ≥25 mm	1 (4.0)
Systemic Adverse Reactions	
Fatigue	8 (32.0)
Headache	5 (20.0)
Myalgia	3 (12.0)
Arthralgia	2 (8.0)
Chills	2 (8.0)
Fever >38.0°C / >100.4°F	1 (4.0)
Fever, Grade 3: 39.0° - 40.0°C / 102.1° - 104.0°F	1 (4.0)
Nausea/vomiting	1 (4.0)
Use of antipyretic or pain medication	6 (24.0)

* 7 days included day of vaccination and the subsequent 6 days. Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary).
† Absence of rows for Grade 3 or Grade 4 adverse reactions indicates no events were reported.

In participants who received a booster dose, the median duration of solicited local and systemic adverse reactions was 3 days.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for up to 28 days following the booster dose. Serious adverse events and medically attended adverse events will be recorded for the entire study duration. As of August 18, 2022, among the 145 participants who had received a booster dose, unsolicited adverse events that occurred within 28 days following vaccination were reported by 24.1% of participants (n=35). In these analyses, 99.3% of study participants had at least 28 days of follow-up. Through the cut-off date, there were no unsolicited adverse events not already captured as solicited local and systemic reactions that were considered causally related to Moderna COVID-19 Vaccine.

Serious Adverse Events

As of August 18, 2022, with a median follow-up duration after the booster dose of 99 days, there were no serious adverse events reported following the booster dose.

Moderna COVID-19 Vaccine Administered as a First Booster Dose Following Primary Vaccination with Another Authorized or Approved COVID-19 Vaccine

The safety of a Moderna COVID-19 Vaccine booster dose in individuals who completed primary vaccination with another authorized or approved COVID-19 vaccine (heterologous booster dose) is inferred from the safety of a Moderna COVID-19 Vaccine booster dose administered following completion of a Moderna COVID-19 Vaccine primary series (homologous booster dose) and from data from an independent Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States that evaluated a booster dose of Moderna COVID-19 Vaccine. The booster dose that study participants received contained twice the amount of mRNA compared to the authorized booster dose of 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. Adverse events were assessed through 28 days after the booster dose. An overall review of adverse reactions reported following the Moderna COVID-19 Vaccine heterologous booster dose did not identify any new safety concerns, as compared with adverse reactions reported following Moderna COVID-19 Vaccine primary series doses or homologous booster dose.

Moderna COVID-19 Vaccine Administered as a Second Booster Dose Following Primary and Booster Vaccination with Another Authorized or Approved COVID-19 Vaccine

In an independently conducted study (*Gili Regev-Yochay, Tal Gonen, Mayan Gilboa, et al. 2022 DOI: 10.1056/NEJMc2202542*), Moderna COVID-19 Vaccine was administered as a second booster dose to 120 participants 18 years of age and older who had received a 2-dose primary series and a first booster dose of Pfizer-BioNTech COVID-19 Vaccine at least 4 months prior. No new safety concerns were reported during up to three weeks of follow-up after the second booster dose.

Bivalent Vaccine (Original and Omicron BA.1) Administered as a Second Booster Dose in Participants 18 Years of Age and Older

Study 5 (NCT04927065), a Phase 2/3 open-label study conducted in the United States, evaluated the immunogenicity, safety, and reactogenicity of a booster dose of the bivalent vaccine (Original and Omicron BA.1) compared to a booster dose of Moderna COVID-19 Vaccine (50 mcg mRNA; previously but no longer authorized for booster vaccination in individuals 18 years of age and older) when administered as a second booster dose to participants 18 years of age and older who had previously received a primary series and a first booster dose with Moderna

COVID-19 Vaccine at least 3 months prior. The bivalent vaccine (Original and Omicron BA.1) contained 25 mcg of mRNA encoding the pre-fusion stabilized S-glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original) and 25 mcg of mRNA encoding the S-glycoprotein of SARS-CoV-2 Omicron variant lineage BA.1, for a total of 50 mcg mRNA per dose. The safety analysis set included 437 participants in the bivalent vaccine (Original and Omicron BA.1) booster dose group and 377 participants in the Moderna COVID-19 Vaccine booster dose group.

The median age of the population was 60 years (range 20-96); 490 (60.2%) participants were 18 years through 64 years of age and 324 (39.8%) were 65 years and older. Overall, 44.8% were male, 55.2% were female, 10.2% were Hispanic or Latino, 86.4% were White, 7.4% were African American, 3.7% were Asian, 0.1% were American Indian or Alaska Native, 0.1% were Native Hawaiian or Pacific Islander, 0.6% were other races, and 1.1% were Multiracial. Demographic characteristics were similar among participants who received the bivalent vaccine (Original and Omicron BA.1) and those who received Moderna COVID-19 Vaccine. Following the booster dose through the cutoff date of April 27, 2022, the median follow-up time was 43 days among bivalent vaccine (Original and Omicron BA.1) recipients and 57 days among Moderna COVID-19 Vaccine recipients.

Unsolicited Adverse Events

Participants were monitored for unsolicited adverse events for up to 28 days following the booster dose. Serious adverse events and medically attended adverse events will be recorded for the entire study duration. As of April 27, 2022, among participants who had received a booster dose (bivalent vaccine [Original and Omicron BA.1]=437, Moderna COVID-19 Vaccine=377), unsolicited adverse events that occurred within 28 days following vaccination were reported by 18.5% of participants (n=81) who received bivalent vaccine (Original and Omicron BA.1) and 20.7% of participants (n=78) who received Moderna COVID-19 Vaccine. In these analyses, 99.9% of study participants had at least 28 days of follow-up after the booster dose. The incidence of unsolicited adverse events was similar between the vaccine groups and no new safety concerns were identified.

Serious Adverse Events

As of April 27, 2022, the median duration of follow-up was 43 days among bivalent vaccine (Original and Omicron BA.1) recipients and 57 days among Moderna COVID-19 Vaccine recipients. Serious adverse events were reported by 0.7% (n=3) of participants who received bivalent vaccine (Original and Omicron BA.1) and 0.3% (n=1) of participants who received Moderna COVID-19 Vaccine. None of the events in the bivalent vaccine (Original and Omicron BA.1) group or Moderna COVID-19 Vaccine group were considered related to vaccine.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of SPIKEVAX, Moderna COVID-19 Vaccine, Moderna COVID-19 Vaccine, Bivalent, and Moderna COVID-19 Vaccine (2023-2024 Formula). Because these reactions are reported voluntarily, it is not always

possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis
Immune System Disorders: anaphylaxis, urticaria
Nervous System Disorders: syncope, febrile seizures

6.3 Required Reporting for Adverse Events and Vaccine Administration Errors

Vaccination providers must report the listed events following administration of the Moderna COVID-19 Vaccine (2024-2025 Formula)[8] 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 myocarditis
- Cases of pericarditis
- Cases of Multisystem Inflammatory Syndrome (MIS)
- Cases of COVID-19 that results in hospitalization or death

*Serious Adverse Events are defined as:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect;
- An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent one of the outcomes listed above.

Instructions for Reporting to VAERS

Vaccination providers should complete and submit a VAERS form to FDA using one of the following methods:

- Complete and submit the report online: https://vaers.hhs.gov/reportevent.html, or
- If you are unable to submit this form electronically, you may fax it to VAERS at 1-877-721-0366. If you need additional help submitting a report, you may call the VAERS toll-free information line at 1-800-822-7967 or send an email to info@vaers.org.

IMPORTANT: When reporting adverse events or vaccine administration errors to VAERS, please complete the entire form with detailed information. It is important that the information reported to FDA be as detailed and complete as possible. Information to include:

- Patient demographics (e.g., patient name, date of birth)

[8] Vaccination providers administering SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) under EUA must adhere to the same reporting requirements.

- Pertinent medical history
- Pertinent details regarding admission and course of illness
- Concomitant medications
- Timing of adverse event(s) in relationship to administration of Moderna COVID-19 Vaccine (2024-2025 Formula)
- Pertinent laboratory and virology information
- Outcome of the event and any additional follow-up information if it is available at the time of the VAERS report. Subsequent reporting of follow-up information should be completed if additional details become available.

The following steps are highlighted to provide the necessary information for safety tracking:

1. In Box 17, provide information on Moderna COVID-19 Vaccine (2024-2025 Formula) and any other vaccines administered on the same day; and in Box 22, provide information on any other vaccines received within one month prior.
2. In Box 18, description of the event:
    a. Write "Moderna COVID-19 Vaccine (2024-2025 Formula) EUA" as the first line
    b. Provide a detailed report of vaccine administration error and/or adverse event. It is important to provide detailed information regarding the patient and adverse event/medication error for ongoing safety evaluation of this unapproved vaccine. Please see information to include listed above.
3. Contact information:
    a. In Box 13, provide the name and contact information of the prescribing healthcare provider or institutional designee who is responsible for the report.
    b. In Box 14, provide the name and contact information of the best doctor/healthcare professional to contact about the adverse event.
    c. In Box 15, provide the address of the facility where vaccine was given (NOT the healthcare provider's office address).

Other Reporting Instructions

Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to ModernaTX, Inc. using the contact information below or by providing a copy of the VAERS form to ModernaTX, Inc.

Website	https://report.moderna.convergehealthsafety.com/
Fax number	1-866-599-1342
Telephone number	1-866-MODERNA (1-866-663-3762)

7 DRUG INTERACTIONS

There are no data to assess the concomitant administration of Moderna COVID-19 Vaccine with other vaccines.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on SPIKEVAX, Moderna COVID-19 Vaccine, Bivalent or Moderna COVID-19 Vaccine administered to pregnant individuals are insufficient to inform vaccine-associated risks in pregnancy.

In a developmental toxicity study, 0.2 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (mRNA) (100 mcg) and other ingredients included in a single primary series dose of Moderna COVID-19 Vaccine for individuals 12 years of age and older was administered to female rats by the intramuscular route on four occasions: 28 and 14 days prior to mating, and on gestation days 1 and 13. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk

Pregnant individuals infected with SARS-CoV-2 are at increased risk of severe COVID-19 compared with non-pregnant individuals.

8.2 Lactation

Risk Summary

It is not known whether Moderna COVID-19 Vaccine is excreted in human milk. Data are not available to assess the effects of Moderna COVID-19 Vaccine on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Moderna COVID-19 Vaccine and any potential adverse effects on the breastfed child from Moderna COVID-19 Vaccine or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Moderna COVID-19 Vaccine is authorized for use in individuals 6 months through 11 years of age.

Moderna COVID-19 Vaccine is not authorized for use in individuals younger than 6 months of age or individuals 12 years of age and older.

8.6 Use in Immunocompromised Individuals

Safety and effectiveness of the Moderna COVID-19 Vaccine in individuals 6 months through 11 years of age with immunocompromise have been extrapolated from adult data. In an independent study (*Hall VG, Ferreira VH, Ku T et al. Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients. N Engl J Med 2021 DOI: 10.1056/NEJMc2111462; NCT04885907*), safety and effectiveness of a third primary series dose of Moderna COVID-19 Vaccine have been evaluated in participants who received solid organ transplants. In this study, in 60 adult participants who had undergone various solid organ transplant procedures (heart, kidney, kidney-pancreas, liver, lung, pancreas) a median of 3.57 years previously (range 1.99-6.75 years) who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no Grade 3 or Grade 4 events were reported. The administration of a third primary series vaccine dose appears to be only moderately effective in increasing antibody titers. Patients should be counseled to maintain physical precautions to help prevent COVID-19. In addition, close contacts of immunocompromised persons should be vaccinated, as appropriate for their health status.

11 DESCRIPTION

Moderna COVID-19 Vaccine is provided as a sterile white to off-white injectable suspension for intramuscular use.

Each 0.25 mL dose of Moderna COVID-19 Vaccine (2024-2025 Formula) contains 25 mcg nucleoside-modified messenger RNA (mRNA) encoding the pre-fusion stabilized Spike glycoprotein (S) of the SARS-CoV-2 Omicron variant lineage KP.2. Each dose also contains the following ingredients: a total lipid content of 0.5 mg (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), 0.13 mg tromethamine, 0.62 mg tromethamine hydrochloride, 0.011 mg acetic acid, 0.049 mg sodium acetate trihydrate, and 21.8 mg sucrose.

Moderna COVID-19 Vaccine (2024-2025 Formula) does not contain a preservative.

The rubber tip cap and plunger used for the single dose syringes are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

The nucleoside-modified mRNA in Moderna COVID-19 Vaccine is formulated in lipid particles, which enable delivery of the nucleoside-modified mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

14 CLINICAL STUDIES

The effectiveness of Moderna COVID-19 Vaccine (2024-2025 Formula) for individuals 6 months through 11 years of age is based on:

- effectiveness of Moderna COVID-19 Vaccine (Original monovalent) in individuals 6 months of age and older, and
- immunogenicity of the bivalent vaccine (Original and Omicron BA.1) in individuals 18 years of age and older

14.1 Efficacy of Two-Dose Primary Series of Moderna COVID-19 Vaccine (Original Monovalent) in Participants 18 Years of Age and Older

Study 1 was a Phase 3 clinical trial with multiple parts. The randomized, placebo-controlled, observer-blind phase evaluated the efficacy, safety, and immunogenicity of Moderna COVID-19 Vaccine in participants 18 years of age and older in the United States. Randomization was stratified by age and health risk: 18 to <65 years of age without comorbidities (not at risk for progression to severe COVID-19), 18 to <65 years of age with comorbidities (at risk for progression to severe COVID-19), and 65 years of age and older with or without comorbidities. Participants who were immunocompromised and those with a known history of SARS-CoV-2 infection were excluded from the study. Participants with no known history of SARS-CoV-2 infection but with positive laboratory results indicative of infection at study entry were included. The study allowed for the inclusion of participants with stable pre-existing medical conditions, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 3 months before enrollment, as well as participants with stable human immunodeficiency virus (HIV) infection. A total of 30,415 participants were randomized equally to receive 2 doses of Moderna COVID-19 Vaccine or saline placebo 1 month apart. Participants will be followed for efficacy and safety until 2 years after the second dose.

The primary efficacy analysis population (referred to as the Per-Protocol Set) included 28,451 participants who received two doses (at 0 and 1 month) of either Moderna COVID-19 Vaccine (100 mcg mRNA per dose; n=14,287) or placebo (n=14,164), and had a negative baseline SARS-CoV-2 status. In the Per-Protocol Set, 47.5% of participants were female, 19.7% were Hispanic or Latino; 79.7% were White, 9.7% were African American, 4.7% were Asian, and 2.0% other races. The median age of participants was 53 years (range 18-95) and 25.4% of participants were 65 years of age and older. Of the study participants in the Per-Protocol Set, 22.8% were at increased risk of severe COVID-19 due to at least one pre-existing medical condition (chronic lung disease, significant cardiac disease, severe obesity, diabetes, liver disease, or HIV infection) regardless of age. There were no notable differences in demographics or pre-existing medical conditions between participants who received Moderna COVID-19 Vaccine and those who

received placebo.

The population for the vaccine efficacy analysis included participants 18 years of age and older who were enrolled from July 27, 2020, and followed for the development of COVID-19 through the data cutoff of March 26, 2021, or the Participant Decision Visit for treatment unblinding, whichever was earlier. The median length of follow-up for participants in the blinded placebo-controlled phase of the study was 4 months following Dose 2.

Efficacy Against COVID-19

COVID-19 was defined based on the following criteria: The participant must have experienced at least two of the following systemic symptoms: fever (≥38ºC / ≥100.4ºF), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s); or the participant must have experienced at least one of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, or clinical or radiographical evidence of pneumonia; and the participant must have at least one NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2 by RT-PCR. COVID-19 cases were adjudicated by a Clinical Adjudication Committee.

There were 55 COVID-19 cases in the Moderna COVID-19 Vaccine group and 744 cases in the placebo group, with a vaccine efficacy of 93.2% (95% confidence interval of 91.0% to 94.8%) (Table 10).

SARS-CoV-2 identified in the majority of COVID-19 cases in this study were sequenced to be the B.1.2 variant. Additional SARS-CoV-2 variants identified in this study included B.1.427/B.1.429 (Epsilon), P.1 (Gamma), and P.2 (Zeta). Representation of identified variants among cases in the vaccine versus placebo recipients did not suggest decreased vaccine effectiveness against these variants.

Table 10: Vaccine Efficacy Against COVID-19* in Participants 18 Years of Age and Older Starting 14 Days After Dose 2 per Adjudication Committee Assessments – Per-Protocol Set

	Moderna COVID-19 Vaccine[a]			Placebo[b]			
Age Subgroup (Years)	**Participants (N)**	**COVID-19 Cases (n)**	**Incidence Rate of COVID-19 per 1,000 Person-Years**	**Participants (N)**	**COVID-19 Cases (n)**	**Incidence Rate of COVID-19 per 1,000 Person-Years**	**% Vaccine Efficacy (95% CI)[c]**
All participants	14,287	55	9.6	14,164	744	136.6	93.2 (91.0, 94.8)
18 to <65	10,661	46	10.7	10,569	644	159.0	93.4 (91.1, 95.1)
	3,626	9	6.2	3,595	100	71.7	91.5 (83.2, 95.7)

* COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least two systemic symptoms (fever [≥38ºC / ≥100.4ºF], chills, myalgia, headache, sore throat, new olfactory and taste disorder[s]) or one respiratory symptom (cough, shortness of breath or difficulty breathing, or clinical or radiographical evidence of pneumonia). Cases starting 14 days after Dose 2.
[a] Moderna COVID-19 Vaccine dosing was a two-dose series (100 mcg mRNA per dose) 1 month apart.
[b] Placebo dosing was a two-dose series (saline solution) 1 month apart.
[c] VE and 95% CI from the stratified Cox proportional hazard model.

Severe COVID-19 was defined based on confirmed COVID-19 as per the primary efficacy endpoint case definition, plus any of the following: Clinical signs indicative of severe systemic illness, respiratory rate ≥30 per minute, heart rate ≥125 beats per minute, SpO2 ≤93% on room air at sea level or PaO2/FIO2 <300 mm Hg; or respiratory failure or ARDS (defined as needing high-flow oxygen, non-invasive or mechanical ventilation, or ECMO), evidence of shock (systolic blood pressure <90 mmHg, diastolic BP <60 mmHg or requiring vasopressors); or significant acute renal, hepatic, or neurologic dysfunction; or admission to an intensive care unit or death.

Among all participants in the Per-Protocol Set analysis, which included COVID-19 cases confirmed by an adjudication committee, 2 cases of severe COVID-19 were reported in the Moderna COVID-19 Vaccine group compared with 106 cases reported in the placebo group, with a vaccine efficacy of 98.2% (95% confidence interval of 92.8% to 99.6%) (Table 11).

Table 11: Vaccine Efficacy Against Severe COVID-19* in Participants 18 Years of Age and Older Starting 14 Days After Dose 2 per Adjudication Committee Assessments – Per-Protocol Set

Moderna COVID-19 Vaccine[a]			Placebo[b]			
Participants (N)	Severe COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	Participants (N)	Severe COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	% Vaccine Efficacy (95% CI)[c]
14,287	2	0.3	14,164	106	19.1	98.2 (92.8, 99.6)

* Severe COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least two systemic symptoms or one respiratory symptom, plus any of the following: Clinical signs indicative of severe systemic illness, respiratory rate ≥30 per minute, heart rate ≥125 beats per minute, SpO2 ≤93% on room air at sea level or PaO2/FIO2 <300 mm Hg; or respiratory failure or ARDS (defined as needing high-flow oxygen, non-invasive or mechanical ventilation, or ECMO), evidence of shock (systolic blood pressure <90 mmHg, diastolic BP <60 mmHg or requiring vasopressors); or significant acute renal, hepatic, or neurologic dysfunction; or admission to an intensive care unit or death. Cases starting 14 days after Dose 2.
[a] Moderna COVID-19 Vaccine dosing was a two-dose series (100 mcg mRNA per dose) 1 month apart.
[b] Placebo dosing was a two-dose series (saline solution) 1 month apart.
[c] VE and 95% CI from the stratified Cox proportional hazard model.

In an exploratory analysis, occurrence of asymptomatic SARS-CoV-2 infection was assessed among participants in the Per-Protocol Set (enrolled from July 27, 2020, and followed maximally through March 26, 2021). Asymptomatic SARS-CoV-2 infection was defined as having a

positive scheduled serology test based on binding antibody against SARS-CoV-2 nucleocapsid protein as measured by the Roche Elecsys immunoassay (N-serology) and/or a positive RT-PCR test for SARS-CoV-2, in the absence of any reported COVID-19 symptoms included as part of the primary efficacy endpoint case definition (described above) or symptoms included in the secondary COVID-19 endpoint case definition (fever ≥38°C / ≥100.4°F, chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches, body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea, vomiting, or diarrhea) at any time during the study. To assess for asymptomatic infection starting 14 days after Dose 2, all participants had scheduled blood draws for N-serology collected at the 1-month post-Dose 2 visit and the 6-month post-Dose 2 visit (if still blinded to treatment arm), and scheduled N-serology and nasopharyngeal swab for RT-PCR collection at the Participant Decision Visit for treatment unblinding.

In the Per-Protocol Set, 14,287 participants in the Moderna COVID-19 Vaccine group and 14,164 participants in the placebo group had N-serology and/or RT-PCR results available from one or more of the pre-specified timepoints listed above. Among these participants, there were 180 cases of asymptomatic SARS-CoV-2 infection in the Moderna COVID-19 Vaccine group compared with 399 cases in the placebo group. Limitations of this analysis include the infrequently scheduled assessments for serology and PCR testing, which may not have captured all cases of asymptomatic infections which occurred during the study.

14.2 Effectiveness of Two-Dose Primary Series of Moderna COVID-19 Vaccine (Original Monovalent) in Participants 12 Years Through 17 Years of Age

Study 3 is an ongoing Phase 3 clinical trial with multiple parts. The randomized, placebo-controlled, observer-blind phase evaluated the safety, reactogenicity, and effectiveness of Moderna COVID-19 Vaccine in participants ages 12 years through 17 years in the United States. Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 3,733 participants were randomized 2:1 to receive 2 doses of Moderna COVID-19 Vaccine (100 mcg mRNA per dose) or saline placebo 1 month apart. Among participants assessed for immunogenicity, 52.4% of participants were male, 47.6% were female, 7.6% were Hispanic or Latino; 83.5% were White, 1.2% were African American, 4.4% were Asian, 0.3% were Native Hawaiian or Pacific Islander, 2.1% were other races, and 5.6% were Multiracial.

Effectiveness in individuals 12 years through 17 years of age is based on a comparison of immune responses in this age group to adults 18 years through 25 years of age.

In Study 3, an analysis was conducted of SARS-CoV-2 50% neutralizing titers and seroresponse rates 28 days after Dose 2 in a subset of participants 12 years through 17 years of age in Study 3 and participants 18 years through 25 years of age in Study 1 who had no immunologic or virologic evidence of prior SARS-CoV-2 at baseline. Noninferior immune responses as assessed by geometric mean 50% neutralizing titers and seroresponse rates were demonstrated in a comparison of participants 12 years through 17 years of age to participants 18 years through 25 years of age (Table 12).

Table 12: Comparison of Geometric Mean Titer Ratio and Seroresponse Rate Against a Pseudovirus Expressing the Original SARS-CoV-2 Spike Protein (D614G) at 28 Days After Completion of the Primary Series of Moderna COVID-19 Vaccine,* Participants 12 Years Through 17 Years of Age vs Participants 18 Years Through 25 Years of Age – Per-Protocol Immunogenicity Subset

12 Years Through 17 Years N=340	18 Years Through 25 Years N=295	12 Years Through 17 Years/ 18 Years Through 25 Years	
GMT (95% CI)[a]	**GMT (95% CI)[a]**	**GMT Ratio (95% CI)[b]**	**Met Success Criteria[c]**
1401.7 (1276.2, 1539.5)	1299.9 (1175.4, 1437.5)	1.1 (0.9, 1.2)	Yes
Seroresponse %[d] (95% CI)[e]	**Seroresponse %[d] (95% CI)[e]**	**Difference in Seroresponse Rate % (95% CI)[f]**	**Met Success Criteria[c]**
98.8 (97.0, 99.7)	99.0 (97.1, 99.8)	-0.2 (-2.1, 1.9)	Yes

N=Number of subjects with non-missing data at the corresponding timepoint.
GMT=Geometric mean titers
***** Moderna COVID-19 Vaccine dosing was a two-dose series (100 mcg mRNA per dose) 1 month apart.
[a] Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.
[b] The log-transformed antibody levels are analyzed using an analysis of covariance (ANCOVA) model with the group variable (adolescents in Study 3 and young adults in Study 1) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.
[c] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMT Ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.
[d] Proportion of participants who met seroresponse definition.
[e] Seroresponse due to vaccination specific to pseudovirus neutralizing antibody ID50 titer at a subject level is defined as at least 4-fold rise from baseline, where baseline titers <LLOQ are set to LLOQ for the analysis. 95% CI is calculated using the Clopper-Pearson method.
[f] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.
Note: SARS-CoV-2 50% inhibitory dose (ID50) neutralization titers were determined using a SARS-CoV-2 Spike-Pseudotyped Virus Neutralization Assay. Quantification of SARS-CoV-2 neutralizing antibodies utilizes lentivirus particles expressing SARS-CoV-2 Spike protein on their surface and contains a firefly luciferase (Luc) reporter gene for quantitative measurements of infection by relative luminescence units (RLU). Neutralization is measured as the serum dilution at which RLU is reduced by 50% (ID50) relative to mean RLU in virus control wells but after subtraction of mean RLU in cell control wells.

A descriptive efficacy analysis evaluating confirmed COVID-19 cases accrued up to the blinded data cutoff date of May 31, 2021, was performed in 3,186 participants who received two doses (at 0 and 1 month) of either Moderna COVID-19 Vaccine (n=2,142) or placebo (n=1,044) and had a negative baseline SARS-CoV-2 status (referred to as the Per-Protocol Set for Efficacy). In the Per-Protocol Set for Efficacy, 51.5% were male, 48.5% were female, 11.0% were Hispanic or Latino; 84.0% were White, 2.7% were African American, 6.2% were Asian, 0.5% were American Indian or Alaska Native, <0.1% were Native Hawaiian or Pacific Islander, 0.9% were other races, and 4.8% were Multiracial. There were no notable differences in demographics

between participants who received Moderna COVID-19 Vaccine and those who received placebo.

The population for the vaccine efficacy analysis included participants 12 years through 17 years of age who were enrolled from December 9, 2020, and followed for the development of COVID-19 through the data cutoff of May 31, 2021. The median length of follow-up for participants in the blinded, placebo-controlled phase of the study was 112 days following Dose 2.

The efficacy information in participants 12 years through 17 years of age is presented in Table 13.

Table 13: Efficacy Analyses: COVID-19 in Participants 12 Years Through 17 Years of Age Starting 14 Days After Dose 2 – Per-Protocol Set for Efficacy

	Moderna COVID-19 Vaccine[a] N=2,142		**Placebo[b]** N=1,044		
	COVID-19 Cases (n)	**Incidence Rate of COVID-19 per 1,000 Person-Years**	**COVID-19 Cases (n)**	**Incidence Rate of COVID-19 per 1,000 Person-Years**	**% Vaccine Efficacy (95% CI)[c]**
COVID-19 Case Definition 1[d]	0	0	6	21.5	100.0 (61.2, NE)
COVID-19 Case Definition 2[e]	2	3.3	9	32.4	89.9 (51.0, 98.9)

NE=Not estimable

[a] Moderna COVID-19 Vaccine dosing was a two-dose series (100 mcg mRNA per dose) 1 month apart.

[b] Placebo dosing was a two-dose series (saline solution) 1 month apart.

[c] Vaccine efficacy defined as 1 - ratio of incidence rate (Moderna COVID-19 Vaccine vs. placebo). The 95% CI of the ratio is calculated using the exact method conditional upon the total number of cases, adjusting for person-years.

[d] COVID-19 Case Definition 1: Participant must have experienced at least two of the following systemic symptoms: fever (≥38°C / ≥100.4°F), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s); or the participant must have experienced at least one of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, or clinical or radiographical evidence of pneumonia; and the participant must have at least one NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS- CoV-2 by RT-PCR.

[e] COVID-19 Case Definition 2: Presence of at least one symptom from a list of COVID-19 symptoms and a positive NP swab or saliva sample for SARS-CoV-2 by RT-PCR. Listed symptoms were fever (temperature >38°C / ≥100.4°F), or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches, or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea, or vomiting or diarrhea.

14.3 Effectiveness of Two-Dose Primary Series of Moderna COVID-19 Vaccine (Original Monovalent) in Participants 6 Years Through 11 Years of Age

Study 4 includes an ongoing Phase 2/3 randomized, placebo-controlled, observer-blind clinical trial component to evaluate the safety, reactogenicity, and effectiveness of Moderna COVID-19 Vaccine in individuals ages 6 years through 11 years in the United States and Canada (NCT04796896). Participants with a known history of SARS-CoV-2 infection within 2 weeks of

study vaccination were excluded from the study. A total of 4,016 participants were randomized 3:1 to receive 2 doses of Moderna COVID-19 Vaccine (50 mcg mRNA per dose) or saline placebo 1 month apart. Participants will be followed for occurrence of COVID-19 and safety until 1 year after the last dose.

Effectiveness in individuals 6 years through 11 years of age is based on a comparison of immune responses in this age group to adults 18 years through 25 years of age.

In Study 4, an analysis was conducted of SARS-CoV-2 50% neutralizing titers and seroresponse rates 28 days after Dose 2 in a subset of individuals 6 years through 11 years of age in Study 4 and participants 18 years through 25 years of age in Study 1 who had no immunologic or virologic evidence of prior SARS-CoV-2 at baseline. Noninferior immune responses as assessed by geometric mean 50% neutralizing titers and seroresponse rates were demonstrated in a comparison of individuals 6 years through 11 years of age to participants 18 years through 25 years of age (Table 14).

Table 14: Summary of Geometric Mean Titer Ratio and Seroresponse Rate – Comparison of Individuals 6 Years Through 11 Years of Age to Participants 18 Years Through 25 Years of Age – Per-Protocol Immunogenicity Set

		Moderna COVID-19 Vaccine			
		6 Years Through 11 Years[a] n=320	18 Years Through 25 Years[b] n=295	6 Years Through 11 Years/ 18 Years Through 25 Years	
Assay	**Time Point**	**GMT (95% CI)[c]**	**GMT (95% CI)[c]**	**GMT ratio (95% CI)[d]**	**Met Noninferiority Objective (Y/N)[e]**
SARS-CoV-2 neutralization assay – ID50 (titer)[f]	28 days after Dose 2	1610.2 (1456.6, 1780.0)	1299.9 (1171.2, 1442.7)	1.2 (1.1, 1.4)	Yes
		Seroresponse % (95% CI)[g]	**Seroresponse % (95% CI)[g]**	**Difference in Seroresponse Rate % (95% CI)[h]**	
		99.1 (97.3, 99.8)	99.0 (97.1, 99.8)	0.1 (-1.9, 2.1)	

GMT=Geometric mean titer

[a] Moderna COVID-19 Vaccine dosing was a two-dose series (50 mcg mRNA per dose) 1 month apart.

[b] Moderna COVID-19 Vaccine dosing was a two-dose series (100 mcg mRNA per dose) 1 month apart.

[c] Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.

[d] The log-transformed antibody levels are analyzed using an analysis of covariance (ANCOVA) model with the group variable (individuals in Study 4 and young adults in Study 1) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.

[e] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMT ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.

[f] SARS-CoV-2 50% inhibitory dose (ID50) neutralization titers were determined using a SARS-CoV-2 Spike-Pseudotyped Virus Neutralization Assay. Quantification of SARS-CoV-2 neutralizing antibodies utilizes lentivirus particles expressing SARS-CoV-2 Spike protein on their surface and contains a firefly luciferase (Luc) reporter

gene for quantitative measurements of infection by relative luminescence units (RLU). Neutralization is measured as the serum dilution at which RLU is reduced by 50% (ID50) relative to mean RLU in virus control wells but after subtraction of mean RLU in cell control wells.

[g] Seroresponse due to vaccination specific to pseudovirus neutralizing antibody ID50 titer at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.

[h] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen method.

In a descriptive analysis, vaccine efficacy could not be determined reliably. An insufficient number of COVID-19 cases were accrued in the Per-Protocol population starting 14 days after Dose 2 due to treatment unblinding and cross-over vaccination after the availability of an authorized COVID-19 vaccine in this age group.

14.4 Effectiveness of Two-Dose Primary Series of Moderna COVID-19 Vaccine (Original Monovalent) in Participants 6 Months Through 5 Years of Age

Study 4 includes an ongoing Phase 2/3 randomized, placebo-controlled, observer-blind clinical trial component to evaluate the safety, reactogenicity, and effectiveness of Moderna COVID-19 Vaccine in individuals ages 6 months through 5 years in the United States and Canada (NCT04796896). Participants with a known history of SARS-CoV-2 infection within 2 weeks of study vaccination were excluded from the study. A total of 6,403 participants were randomized 3:1 to receive 2 doses of the Moderna COVID-19 Vaccine (25 mcg mRNA per dose) or saline placebo 1 month apart. Participants will be followed for occurrence of COVID-19 and safety until 1 year after the last dose.

Effectiveness in individuals 6 months through 5 years of age is based on a comparison of immune responses in this age group to adults 18 years through 25 years of age.

In Study 4, an analysis was conducted of SARS-CoV-2 neutralizing antibody concentrations and seroresponse rates 28 days after Dose 2 in a subset of individuals 6 months through 5 years of age in Study 4 and participants 18 years through 25 years of age in Study 1 who had no immunologic or virologic evidence of prior SARS-CoV-2 at baseline. Noninferior immune responses as assessed by neutralizing antibody concentrations in arbitrary units (AU)/mL and seroresponse rates were demonstrated in a comparison of individuals 6 months through 23 months of age to participants 18 years through 25 years of age (Table 15) and 2 years through 5 years of age to participants 18 years through 25 years of age (Table 16).

Table 15: Summary of Geometric Mean Concentration Ratio and Seroresponse Rate – Comparison of Individuals 6 Months Through 23 Months of Age to Participants 18 Years Through 25 Years of Age – Per-Protocol Immunogenicity Set

		Moderna COVID-19 Vaccine			
		6 Months Through 23 Months[a] n=230	18 Years Through 25 Years[b] n=291	6 Months Through 23 Months/ 18 Years Through 25 Years	
Assay	**Time Point**	**GMC (95% CI)[c]**	**GMC (95% CI)[c]**	**GMC Ratio (95% CI)[d]**	**Met Noninferiority Objective (Y/N)[e]**
SARS-CoV-2 neutralization assay[f]	28 days after Dose 2	1780.7 (1606.4, 1973.8)	1390.8 (1269.1, 1524.2)	1.3 (1.1, 1.5)	Yes
		Seroresponse % (95% CI)[g]	**Seroresponse % (95% CI)[g]**	**Difference in Seroresponse Rate % (95% CI)[h]**	
		100 (98.4, 100)	99.3 (97.5, 99.9)	0.7 (-1.0, 2.5)	

n=Number of participants with non-missing data at baseline and at Day 57.
GMC=Geometric mean concentration
[a] Moderna COVID-19 Vaccine dosing was a two-dose series (25 mcg mRNA per dose) 1 month apart.
[b] Moderna COVID-19 Vaccine dosing was a two-dose series (100 mcg mRNA per dose) 1 month apart.
[c] Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.
[d] The log-transformed antibody levels are analyzed using an analysis of covariance (ANCOVA) model with the group variable (individuals in Study 4 and young adults in Study 1) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.
[e] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMC ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.
[f] Final geometric mean antibody concentrations (GMC) in AU/mL were determined using SARS-CoV-2 microneutralization assay. The SARS-CoV-2 MN is a cell-based assay that is designed to determine the ability of SARS-CoV-2 neutralizing antibodies to inhibit the infection of 293T-ACE2 cells by SARS-CoV-2 Reporter Virus Particles (RVP) which express green fluorescent protein (GFP). A given serum sample is pre-incubated with a known quantity of SARS-CoV-2-GFP for 60 (±5) minutes prior to infection of 293T-ACE2 cells. COVID-19 infection is monitored 48 (±4) hours following infection by counting the number of green fluorescent cells using the Cytation 5 cell imaging reader.
[g] Seroresponse due to vaccination specific to SARS-CoV-2 RVP neutralizing antibody concentration at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.
[h] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Table 16: Summary of Geometric Mean Concentration Ratio and Seroresponse Rate – Comparison of Individuals 2 Years Through 5 Years of Age to Participants 18 Years Through 25 Years of Age – Per-Protocol Immunogenicity Set

		Moderna COVID-19 Vaccine			
		2 Years Through 5 Years[a] n=264	18 Years Through 25 Years[b] n=291	2 Years Through 5 Years/ 18 Years Through 25 Years	
Assay	**Time Point**	**GMC (95% CI)[c]**	**GMC (95% CI)[c]**	**GMC Ratio (95% CI)[d]**	**Met Noninferiority Objective (Y/N)[e]**
SARS-CoV-2 neutralization assay[f]	28 days after Dose 2	1410.0 (1273.8, 1560.8)	1390.8 (1262.5, 1532.1)	1.0 (0.9, 1.2)	Yes
		Seroresponse % (95% CI)[g]	**Seroresponse % (95% CI)[g]**	**Difference in Seroresponse Rate % (95% CI)[h]**	
		98.9 (96.7, 99.8)	99.3 (97.5, 99.9)	-0.4 (-2.7, 1.5)	

n=Number of participants with non-missing data at baseline and at Day 57.
GMC=Geometric mean concentration
[a] Moderna COVID-19 Vaccine dosing was a two-dose series (25 mcg mRNA per dose) 1 month apart.
[b] Moderna COVID-19 Vaccine dosing was a two-dose series (100 mcg mRNA per dose) 1 month apart.
[c] Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available.
[d] The log-transformed antibody levels are analyzed using an analysis of covariance (ANCOVA) model with the group variable (individuals in Study 4 and young adults in Study 1) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.
[e] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMC ratio is greater than 0.67, with a point estimate of >0.8 and the lower bound of the 2-sided 95% CI for difference in seroresponse rate is greater than -10%, with a point estimate of >-5%.
[f] Final geometric mean antibody concentrations (GMC) in AU/mL were determined using SARS-CoV-2 microneutralization assay. The SARS-CoV-2 MN is a cell-based assay that is designed to determine the ability of SARS-CoV-2 neutralizing antibodies to inhibit the infection of 293T-ACE2 cells by SARS-CoV-2 Reporter Virus Particles (RVP) which express green fluorescent protein (GFP). A given serum sample is pre-incubated with a known quantity of SARS-CoV-2-GFP for 60 (±5) minutes prior to infection of 293T-ACE2 cells. COVID-19 infection is monitored 48 (±4) hours following infection by counting the number of green fluorescent cells using the Cytation 5 cell imaging reader.
[g] Seroresponse due to vaccination specific to SARS-CoV-2 RVP neutralizing antibody concentration at a subject level is defined in protocol as a change from below LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline is equal to or above LLOQ. Seroresponse 95% CI is calculated using the Clopper-Pearson method.
[h] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

A descriptive efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date February 21, 2022, was performed in 5,476 participants 6 months through 5 years of age who received two doses (at 0 and 1 month) of either Moderna COVID-19 Vaccine or placebo and had a negative baseline SARS-CoV-2 status (referred to as the Per-Protocol Set for Efficacy) (for participants 6 months through 23 months, vaccine=1,511, placebo=513; for participants 2 years through 5 years, vaccine=2,594, placebo=858). For participants 6 months through 23 months in the Per-Protocol Set for Efficacy, 51.2% were male, 48.8% were female,

12.7% were Hispanic or Latino; 78.9% were White, 3.1% were African American, 4.6% were Asian, 0.2% were American Indian or Alaska Native, 0.0% were Native Hawaiian or Pacific Islander, 1.8% were other races, and 10.7% were Multiracial. For participants 2 years through 5 years, 50.7% were male, 49.3% were female, 14.0% were Hispanic or Latino, 76.8% were White, 4.1% were African American, 6.1% were Asian, 0.4% were American Indian or Alaska Native, 0.3% were Native Hawaiian or Pacific Islander, 1.6% were other races, and 10.3% were Multiracial. Between participants who received Moderna COVID-19 Vaccine and those who received placebo, there were no notable differences in demographics.

The median length of follow-up for efficacy post-Dose 2 was 68 days for participants 6 months through 23 months of age and 71 days for participants 2 years through 5 years of age.

Vaccine efficacy among individuals 6 months through 5 years of age in Study 4 was evaluated during the period when the B.1.1.529 (Omicron) variant was the predominant variant in circulation.

The efficacy information in individuals 6 months through 23 months of age and 2 years through 5 years of age are presented in Table 17 and Table 18, respectively.

Table 17: Efficacy Analyses: COVID-19 in Participants 6 Months Through 23 Months of Age Starting 14 Days After Dose 2 – Per Protocol Set for Efficacy

	Moderna COVID-19 Vaccine[a] N=1,511		**Placebo[b]** N=513		
	Cases (n)	**Incidence Rate of COVID-19 per 1,000 Person-Years**	**Cases (n)**	**Incidence Rate of COVID-19 per 1,000 Person-Years**	**% Vaccine Efficacy (95% CI)[c]**
COVID-19 Cases - Definition 1[d]	37	99.981	18	146.042	31.5 (-27.7, 62.0)
COVID-19 Cases - Definition 2[e]	51	138.239	34	279.822	50.6 (21.4, 68.6)

N=Included 15 individuals aged 2 years to 4 years randomized in the 6 months through 23 months of age group stratum (12 in the Moderna COVID-19 Vaccine group and 3 in the placebo group), and none of them had a COVID-19 case starting 14 days after Dose 2.

[a] Moderna COVID-19 Vaccine dosing was a two-dose series (25 mcg mRNA per dose) 1 month apart.

[b] Placebo dosing was a two-dose series (saline solution) 1 month apart.

[c] Vaccine efficacy defined as 1 - ratio of incidence rate (Moderna COVID-19 Vaccine vs. placebo). The 95% CI of the ratio is calculated using the exact method conditional upon the total number of cases, adjusting for person-years.

[d] Participant must have experienced at least two of the following systemic symptoms: fever (≥38°C / ≥100.4°F), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s); or the participant must have experienced at least one of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, or clinical or radiographical evidence of pneumonia; and the participant must have at least one NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2 by RT-PCR.

[e] Presence of at least one symptom from a list of COVID-19 symptoms and a positive NP swab or saliva sample for SARS-CoV-2 by RT-PCR. Listed symptoms were fever (temperature >38°C / ≥100.4°F), or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches, or body aches, headache, new loss of taste or

smell, sore throat, congestion or runny nose, nausea, abdominal pain, poor appetite/poor feeding, or vomiting or diarrhea.

Table 18: Efficacy Analyses: COVID-19 in Participants 2 Years Through 5 Years of Age Starting 14 Days After Dose 2 – Per-Protocol Set for Efficacy

	Moderna COVID-19 Vaccine[a] N=2,594		Placebo[b] N=858		
	Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	% Vaccine Efficacy (95% CI)[c]
COVID-19 Cases - Definition 1[d]	71	103.761	43	193.528	46.4 (19.8, 63.8)
COVID-19 Cases - Definition 2[e]	119	175.023	61	276.980	36.8 (12.5, 54.0)

N=Included 25 individuals younger than 2 years of age randomized in the 2 years through 5 years of age group stratum (18 in the Moderna COVID-19 Vaccine group and 7 in the placebo group), and one in each treatment group had a COVID-19 case starting 14 days after Dose 2.

[a] Moderna COVID-19 Vaccine dosing was a two-dose series (25 mcg mRNA per dose) 1 month apart.

[b] Placebo dosing was a two-dose series (saline solution) 1 month apart.

[c] Vaccine efficacy defined as 1 - ratio of incidence rate (Moderna COVID-19 Vaccine vs. placebo). The 95% CI of the ratio is calculated using the exact method conditional upon the total number of cases, adjusting for person-years.

[d] Participant must have experienced at least two of the following systemic symptoms: fever (≥38°C / ≥100.4°F), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s); or the participant must have experienced at least one of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, or clinical or radiographical evidence of pneumonia; and the participant must have at least one NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2 by RT-PCR.

[e] Presence of at least one symptom from a list of COVID-19 symptoms and a positive NP swab or saliva sample for SARS-CoV-2 by RT-PCR. Listed symptoms were fever (temperature >38°C / ≥100.4°F), or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches, or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea, abdominal pain, poor appetite/poor feeding, or vomiting or diarrhea.

14.5 Immunogenicity of Moderna COVID-19 Vaccine (Original Monovalent) Booster Dose Following Moderna COVID-19 Vaccine (Original Monovalent) Primary Series in Participants 6 Years Through 11 Years of Age

Effectiveness of a booster dose of Moderna COVID-19 Vaccine in participants 6 years through 11 years of age was based on a comparison of immune responses, as assessed by neutralizing antibody concentration against a pseudovirus expressing the SARS-CoV-2 Spike protein from a USA_WA1/2020 isolate carrying the D614G mutation, following the booster dose in this age group to that following the primary series in adults 18 years through 25 years.

In an open-label phase of Study 4, participants 6 years through 11 years of age received a single booster dose of Moderna COVID-19 Vaccine (25 mcg mRNA) at least 6 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity

analysis population included 95 booster dose participants in Study 4 and a random subset of 295 participants 18 years through 25 years of age from Study 1 who received two doses of Moderna COVID-19 Vaccine 1 month apart. Study 1 and Study 4 participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively. Among participants 6 years through 11 years of age assessed for immunogenicity, 48.4% were male, 51.6% were female, 15.8% were Hispanic or Latino; 76.8% were White, 5.3% were Black or African American, 5.3% were Asian, 1.1% were American Indian or Alaskan Native, 1.1% were Native Hawaiian or Pacific Islander, 0.0% were other races, and 7.4% were Multiracial.

The primary immunogenicity analyses of the GMC ratio and difference in seroresponse rates following the booster dose in Study 4 compared to following the primary series in Study 1 met the pre-defined immunobridging success criteria. Seroresponse for a participant was defined as achieving a ≥4-fold rise of neutralizing antibody concentration from baseline (before the first dose of the primary series in Study 4 and Study 1). These analyses are summarized in Table 19.

Table 19: Comparison of Geometric Mean Concentration and Seroresponse Rate Against a Pseudovirus Expressing the SARS-CoV-2 Spike Protein (USA_WA1/2020 isolate carrying the D614G mutation) at 28 Days After a Booster Dose in Study 4 (Participants 6 Years Through 11 Years of Age) vs 28 Days After Completion of the Primary Series in Study 1 (Participants 18 Years Through 25 Years of Age) – Per-Protocol Immunogenicity Subsets

Study 4[a] Booster Dose[b] N=95 GMC (95% CI)	**Study 1[c] Primary Series[d] N=294 GMC (95% CI)**	**GMC Ratio (Study 4/Study 1)**	**Met Success Criterion**
5848 (5000, 6839)	1400 (1281, 1531)	4.2 (3.5, 5.0)	Yes[e]
Study 4 Booster Dose[b] Seroresponse[f] N=95 n/N1 (%) (95% CI)[g]	**Study 1 Primary Series[d] Seroresponse[f] N=294 n/N1 (%) (95% CI)[g]**	**Difference in Seroresponse Rate (Study 4-Study 1) % (95% CI)[h]**	**Met Success Criterion**
88/88 (100) (95.9, 100)	292/294 (99.3) (97.6, 99.9)	0.7 (-3.5, 2.4)	Yes[i]

N=Number of subjects with non-missing data at the corresponding timepoint.
n=Number of participants who achieved seroresponse at 28 days post-Booster Dose for Study 4 or 28 days post-Dose 2 for Study 1.
N1=Number of participants with non-missing data at pre-vaccination baseline and 28 days post-Booster Dose for Study 4 or 28 days post-Dose 2 for Study 1.
[a] Per-Protocol Immunogenicity Subset – Pre-Booster SARS-CoV-2 Negative for Study 4 included all subjects who had both pre-booster and post-booster immunogenicity samples, did not have SARS-CoV-2 infection at pre-booster, did not have a major protocol deviation that impacted immune response, and had post-booster immunogenicity assessment at timepoint of primary interest (28 days post-Booster Dose).
[b] Moderna COVID-19 Vaccine dosing was a single booster dose (25 mcg mRNA).

[c] Per-Protocol Immunogenicity Subset for Study 1 included all subjects who had both baseline (pre-vaccination) and post-vaccination immunogenicity samples, did not have SARS-CoV-2 infection at baseline, did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest (28 days post-Dose 2).
[d] Moderna COVID-19 Vaccine dosing was a two-dose series (100 mcg mRNA per dose) 1 month apart.
[e] Immunobridging success is declared if the lower limit of the 2-sided 95% CI for the GMC Ratio is ≥0.667.
[f] Seroresponse is defined as ≥4-fold rise of pseudovirus neutralizing antibody concentration from baseline (pre-Dose 1 of primary series in Study 4 and Study 1), where baseline concentration < LLOQ is set to LLOQ for the analysis.
[g] 95% CI is calculated using the Clopper-Pearson method.
[h] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.
[i] Immunobridging success is declared if the lower limit of the 2-sided 95% CI for the percentage difference is ≥-10%.
Note: Antibody values < the lower limit of quantitation (LLOQ) are replaced by 0.5 × LLOQ. Values > the upper limit of quantitation (ULOQ) are replaced by the ULOQ if actual values are not available.

A descriptive analysis evaluated seroresponse rates using pre-booster neutralizing antibody concentration. The booster dose seroresponse rate, with seroresponse defined as at least a 4-fold rise relative to the pre-booster concentration, was 92.6%. The difference in seroresponse rates in this post-hoc analysis was -6.7% (95% CI -13.8, -2.7).

14.6 Immunogenicity of Moderna COVID-19 Vaccine (Original Monovalent) Booster Dose Following Moderna COVID-19 Vaccine (Original Monovalent) Primary Series in Participants 17 Months Through 5 Years of Age

Effectiveness of a booster dose of Moderna COVID-19 Vaccine in individuals 6 months through 5 years of age is based on a comparison of immune responses, as assessed by neutralizing antibody concentration against a pseudovirus expressing the SARS-CoV-2 Spike protein from a USA_WA1/2020 isolate carrying the D614G mutation, following the booster dose in study participants 17 months through 5 years of age to that following the primary series in adults 18 years through 25 years of age.

In an open-label phase of Study 4, participants 17 months through 5 years of age received a single booster dose of Moderna COVID-19 Vaccine (10 mcg mRNA) at least 6 months after completion of a Moderna COVID-19 Vaccine primary series (two doses 1 month apart). The primary immunogenicity analysis population included 56 booster dose participants in Study 4 and a random subset of 295 participants 18 years through 25 years of age from Study 1 who had completed primary vaccination with two doses of Moderna COVID-19 Vaccine (100 mcg mRNA per dose) 1 month apart. Study 1 and Study 4 participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively. Among participants 17 months through 5 years of age assessed for immunogenicity, 50.0% were male, 50.0% were female, 7.1% were Hispanic or Latino; 78.6% were White, 1.8% were Black or African American, 7.1% were Asian, 0.0% were American Indian or Alaskan Native, 0.0% were Native Hawaiian or Pacific Islander, 3.6% were other races, and 8.9% were Multiracial. Among the 56 participants in the primary immunogenicity analysis population, the median age for receipt of the booster dose was 2.3 years (range 1.4-5.6 years).

The primary immunogenicity analyses of the GMC ratio and difference in seroresponse rates following the booster dose in Study 4 compared to following the primary series in Study 1 met

the pre-defined immunobridging success criteria. Seroresponse for a participant was defined as achieving a ≥4-fold rise of neutralizing antibody concentration from baseline (before the first dose of the primary series in Study 4 and Study 1). These analyses are summarized in Table 20.

Table 20: Comparison of Geometric Mean Concentration and Seroresponse Rate Against a Pseudovirus Expressing the SARS-CoV-2 Spike Protein (USA_WA1/2020 isolate carrying the D614G mutation) at 28 Days After a Booster Dose in Study 4 (Participants 17 Months Through 5 Years of Age) vs 28 Days After Completion of the Primary Series in Study 1 (Participants 18 Years Through 25 Years of Age) – Per-Protocol Immunogenicity Subsets

Study 4[a] Booster Dose N=56 GMC (95% CI)	**Study 1[c] Primary Series[d] N=294 GMC (95% CI)**	**GMC Ratio (Study 4/Study 1)**	**Met Success Criterion**
5713 (4604, 7089)	1400 (1275, 1539)	4.1 (3.2, 5.2)	Yes[e]
Study 4 Booster Dose Seroresponse[f] N=56 n/N1 (%) (95% CI)[g]	**Study 1 Primary Series Seroresponse[f] N=294 n/N1 (%) (95% CI)[g]**	**Difference in Seroresponse Rate (Study 4-Study 1) % (95% CI)[h]**	**Met Success Criterion**
53/53 (100) (93.3, 100.0)	292/294 (99.3) (97.6, 99.9)	0.7 (-6.1, 2.4)	Yes[i]

N=Number of subjects with non-missing data at the corresponding timepoint.
n=Number of participants who achieved seroresponse at 28 days post-Booster Dose for Study 4 or 28 days post-Dose 2 for Study 1.
N1=Number of participants with non-missing data at pre-vaccination baseline and 28 days post-Booster Dose for Study 4 or 28 days post-Dose 2 for Study 1.
[a] Per-Protocol Immunogenicity Subset – Pre-Booster SARS-CoV-2 Negative for Study 4 included all subjects who had both pre-booster and post-booster immunogenicity samples, did not have SARS-CoV-2 infection at pre-booster, did not have a major protocol deviation that impacted immune response, and had post-booster immunogenicity assessment at timepoint of primary interest (28 days post-Booster Dose).
[b] Moderna COVID-19 Vaccine dosing was a single booster dose (10 mcg mRNA).
[c] Per-Protocol Immunogenicity Subset for Study 1 included all subjects who had both baseline (pre-vaccination) and post-vaccination immunogenicity samples, did not have SARS-CoV-2 infection at baseline, did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest (28 days post-Dose 2).
[d] Moderna COVID-19 Vaccine dosing was a two-dose series (100 mcg mRNA per dose) 1 month apart.
[e] Immunobridging success is declared if the lower limit of the 2-sided 95% CI for the GMC Ratio is ≥0.667.
[f] Seroresponse is defined as ≥4-fold rise of pseudovirus neutralizing antibody concentration from baseline (pre-Dose 1 of primary series in Study 4 and Study 1), where baseline concentration < LLOQ is set to LLOQ for the analysis.
[g] 95% CI is calculated using the Clopper-Pearson method.
[h] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.
[i] Immunobridging success is declared if the lower limit of the 2-sided 95% CI for the percentage difference is ≥-10%.
Note: Antibody values < the lower limit of quantitation (LLOQ) are replaced by 0.5 × LLOQ. Values > the upper limit of quantitation (ULOQ) are replaced by the ULOQ if actual values are not available.

In a descriptive analysis, the booster dose seroresponse rate among participants 17 months through 5 years of age, with seroresponse defined as at least a 4-fold rise relative to the pre-booster concentration, was 94.6%. The difference in seroresponse rates (Study 4 participants minus Study 1 participants) in this post-hoc analysis was -4.7% (95% CI -14.0, -0.9).

14.7 Immunogenicity of Moderna COVID-19 Vaccine Administered as a First Booster Dose Following Primary Vaccination with Another Authorized or Approved COVID-19 Vaccine

Effectiveness of a Moderna COVID-19 Vaccine booster dose in individuals who completed primary vaccination with another authorized or approved COVID-19 vaccine (heterologous booster dose) is inferred from immunogenicity data supporting effectiveness of a Moderna COVID-19 Vaccine 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 of the Moderna COVID-19 Vaccine. The booster dose that study participants received contained twice the amount of mRNA compared to the authorized booster dose 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 was demonstrated regardless of the vaccine used for primary vaccination.

14.8 Immunogenicity of Bivalent Vaccine (Original and Omicron BA.1) Administered as a Second Booster Dose in Participants 18 Years of Age and Older

Study 5 was a Phase 2/3 open-label study in which participants 18 years of age and older, who had previously received a two-dose primary series and one booster dose of Moderna COVID-19 Vaccine, received a second booster dose with the bivalent vaccine (Original and Omicron BA.1) at least 3 months after the first booster dose. The bivalent vaccine (Original and Omicron BA.1) contained a total of 50 mcg mRNA per dose. The primary immunogenicity analysis population included 334 participants who received a booster dose of bivalent vaccine (Original and Omicron BA.1) and 260 participants who received a booster dose of Moderna COVID-19 Vaccine. Participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the second booster dose.

Among participants assessed for immunogenicity, the median age of the population was 62 years (range 20-96). For the bivalent vaccine (Original and Omicron BA.1) group, 195 (58.4%) participants were age 18 years through 64 years of age and 139 (41.6%) were 65 years of age and older; 43.4% were male, 56.6% were female, 7.2% were Hispanic or Latino, 87.1% were White,

7.2% were African American, 3.3% were Asian, 0.0% were American Indian or Alaska Native, 0.0% were Native Hawaiian or Pacific Islander, 0.6% were other races, and 1.8% were Multiracial. For the Moderna COVID-19 Vaccine group, 140 (53.8%) of participants were age 18 years through 64 years of age and 120 (46.2%) were 65 years of age and older; 48.5% of participants were male, 51.5% were female, 8.5% were Hispanic or Latino, 90.0% were White, 4.2% were African American, 4.2% were Asian, 0.0% were American Indian or Alaska Native, 0.0% were Native Hawaiian or Pacific Islander, 0.4% were other races, and 0.0% were Multiracial. Demographic characteristics were similar among participants who received bivalent vaccine (Original and Omicron BA.1) and those who received Moderna COVID-19 Vaccine.

In Study 5, the neutralizing antibody titers (50% inhibitory dose [ID50]) against a pseudovirus expressing the original SARS-CoV-2 Spike protein (D614G) and a pseudovirus expressing the Omicron BA.1 Spike protein were evaluated. Primary immunogenicity analyses compared the ID50 GMTs and seroresponse rates (the proportion achieving a ≥4-fold rise in ID50 from pre-dose 1 of the primary series) 28 days following a second booster dose with bivalent vaccine (Original and Omicron BA.1) to those following a second booster dose with Moderna COVID-19 Vaccine. Analyses of GMTs met predefined success criteria for superiority against Omicron BA.1 and noninferiority against the Original strain. The analysis of seroresponse against Omicron BA.1 met the criterion for noninferiority: Lower limit of the 2-sided 97.5% CI for the percentage difference in seroresponse rate (bivalent vaccine [Original and Omicron BA.1] minus Moderna COVID-19 Vaccine) >-10%. Table 21 presents the analyses of ID50 GMTs; the primary analysis of seroresponse is not shown.

Post-hoc analyses evaluated the differences in seroresponse rates (the proportion achieving a ≥4-fold rise in ID50 from pre-second booster) against both the Original strain and Omicron BA.1 (Table 22).

Table 21: Neutralizing Antibody Titers (ID50) at 28 Days After a Second Booster Dose with Bivalent Vaccine (Original and Omicron BA.1) or Moderna COVID-19 Vaccine in Participants 18 Years of Age and Older – Per-Protocol Immunogenicity SARS-CoV-2 Negative Set*

Assay	Bivalent Vaccine (Original and Omicron BA.1)[a] N=334 GMT[b] (95% CI)	Moderna COVID-19 Vaccine[c] N=260 GMT[b] (95% CI)	GMT Ratio[b] (Bivalent Vaccine [Original and Omicron BA.1]/Moderna COVID-19 Vaccine) (97.5% CI)	Met Success Criteria
Omicron BA.1	2479.9 (2264.5, 2715.8)	1421.2 (1283.0, 1574.4)	1.7 (1.5, 2.0)	Lower limit of 97.5% CI >1 Criterion: Yes[d]
Original SARS-CoV-2 (D614G)	6422.3 (5990.1, 6885.7)	5286.6 (4887.1, 5718.9)	1.2 (1.1, 1.4)	Lower limit of 97.5% CI ≥0.67 Criterion: Yes[e]

* Per-Protocol Immunogenicity SARS-CoV-2 Negative Set included all subjects who received the planned dose of study vaccine per schedule, had pre-booster and Day 29 neutralizing antibody data against Omicron BA.1, had no

major protocol deviations that impact key or critical data, had no history of HIV infection, and had no serologic or virologic evidence of SARS-CoV-2 infection prior to the second booster dose.

[a] Bivalent vaccine (Original and Omicron BA.1) dosing was a single booster dose (50 mcg mRNA).

[b] The log-transformed antibody levels are analyzed using an analysis of covariance (ANCOVA) model with the treatment variable as fixed effect, adjusting for age group (<65, ≥65 years) and pre-booster antibody titer level (in log 10 scale). The treatment variable corresponds to each individual study arm dose. The resulted least square (LS) means, difference of LS means, and confidence intervals are back transformed to the original scale for presentation.

[c] Moderna COVID-19 Vaccine dosing was a single booster dose (50 mcg mRNA).

[d] Superiority is declared if the lower limit of the 2-sided 97.5% CI for the GMT ratio is >1.

[e] Noninferiority is declared if the lower limit of the 2-sided 97.5% CI for the GMT ratio is ≥0.67.

Note: Antibody values < the lower limit of quantitation (LLOQ) are replaced by 0.5 × LLOQ. Values > the upper limit of quantitation (ULOQ) are replaced by the ULOQ if actual values are not available.

Table 22: Post-hoc Analyses of Seroresponse Rates at 28 Days After a Second Booster Dose with Bivalent Vaccine (Original and Omicron BA.1) or Moderna COVID-19 Vaccine in Participants 18 Years of Age and Older – Per-Protocol Immunogenicity SARS-CoV-2 Negative Set*

Assay	Bivalent Vaccine (Original and Omicron BA.1)[a] Seroresponse[b] N=334 n/N1 (%) (95% CI)[c]	Moderna COVID-19 Vaccine[d] Seroresponse[b] N=260 n/N1 (%) (95% CI)[c]	Difference in Seroresponse Rate (Bivalent Vaccine [Original and Omicron BA.1]-Moderna COVID-19 Vaccine) % (97.5% CI)[e]
Omicron BA.1	250/334 (74.9) (69.8, 79.4)	138/260 (53.1) (46.8, 59.3)	21.6 (12.9, 30.3)
Original SARS-CoV-2 (D614G)	180/334 (53.9) (48.4, 59.3)	111/260 (42.7) (36.6, 49.0)	11.2 (2.1, 20.3)

* Per-Protocol Immunogenicity SARS-CoV-2 Negative Set included all subjects who received the planned dose of study vaccine per schedule, had pre-booster and Day 29 neutralizing antibody data against Omicron BA.1, had no major protocol deviations that impact key or critical data, had no history of HIV infection, and had no serologic or virologic evidence of SARS-CoV-2 infection prior to the second booster dose.

n=Number of participants who achieved seroresponse at 28 days after booster dose.

N1=Number of participants with non-missing data at pre-booster baseline and 28 days after second booster dose.

[a] Bivalent vaccine (Original and Omicron BA.1) dosing was a single booster dose (50 mcg mRNA).

[b] For post-hoc assessment of seroresponse rates, baseline was pre-second booster dose; seroresponse was defined as a change from below the LLOQ to equal or above 4 x LLOQ if participant pre-second booster dose baseline was below the LLOQ, or at least a 4-fold rise if baseline is equal to or above the LLOQ.

[c] 95% CI is calculated using the Clopper-Pearson method.

[d] Moderna COVID-19 Vaccine dosing was a single booster dose (50 mcg mRNA).

[e] Common risk difference and 97.5% CI is calculated using the stratified Miettinen-Nurminen method to adjust for age group (<65, ≥65 years).

14.9 Immunogenicity of a Single Dose of Moderna COVID-19 Vaccine (Original Monovalent) in Participants 6 Years of Age and Older with Evidence of Prior SARS-CoV-2 Infection

Seroprevalence surveys estimate that almost all of the U.S. population 5 years of age and older now have antibodies (from vaccination and/or infection) against SARS-CoV-2 (*Centers for Disease Control and Prevention. COVID Data Tracker. Atlanta, GA: US Department of Health and Human Services, CDC; 2023, March 31. https://covid.cdc.gov/covid-data-tracker*).

A comparison of neutralizing antibody titers against a pseudovirus expressing the original SARS-CoV-2 Spike protein (D614G) at baseline (pre-Dose 1), at 28 days after Dose 1 for participants with evidence of prior SARS-CoV-2 infection, and at 28 days after Dose 2 for participants without evidence of prior SARS-CoV-2 infection from clinical studies evaluating a primary series of Moderna COVID-19 Vaccine is shown in Table 23 for the following age groups: 6 years through 11 years of age and 18 years of age and older. In both age groups, neutralizing antibody titers at 28 days post-Dose 1 in participants with evidence of prior infection were not statistically different from those of participants without evidence of prior infection at 28 days post-Dose 2. The effectiveness of a single dose of Moderna COVID-19 Vaccine in individuals 5 years of age with prior evidence of infection is extrapolated from these data in participants 6 years through 11 years of age.

Table 23: Geometric Mean Antibody Titers Against a Pseudovirus Expressing the SARS-CoV-2 Spike Protein (USA_WA1/2020 isolate carrying the D614G mutation) 28 Days Post-Dose 1 of Moderna COVID-19 Vaccine in Participants With Evidence of Prior SARS-CoV-2 Infection and 28 Days Post-Dose 2 of Moderna COVID-19 Vaccine in Participants Without Evidence of Prior SARS-CoV-2 Infection

	Study 4 6 Years Through 11 Years (50 mcg mRNA)		Study 1 Years (100 mcg mRNA)	
Baseline SARS-CoV-2 status	Positive[a]	Negative[b]	Positive[a]	Negative[b]
Baseline GMT	(n=15) 59.4	(n=318) 9.3	(n=130) 68.1	(n=1,050) 9.6
Timepoint	28 days post-Dose 1	28 days post-Dose 2	28 days post-Dose 1	28 days post-Dose 2
Post-Vaccination GMT (95% CI)	(n^1=15) 2110.0 (845.1, 5268.4)	(n^1=321) 1616.5 (1463.1, 1786.1)	(n^1=130) 1478.9 (1069.6, 2044.9)	(n^1=1,053) 1081.1 (1019.8, 1146.1)

Populations used for the analyses were the Immunogenicity Subset for Study 4 and the Per Protocol Random Subcohort for Immunogenicity (PPRSI) for Study 1. The immunogenicity subset for Study 4 consisted of randomized participants who had received at least one dose of study intervention and were included in the subset selected for immunogenicity sampling and testing. The PPRSI for Study 1 consisted of all participants who were included in the random subcohort and who had received both planned doses of study intervention as scheduled and had no major protocol deviations.
n=Number of participants with non-missing data at both baseline and post-vaccination specific timepoint.
n^1=Number of participants with non-missing data at the corresponding post-vaccination timepoint.

[a] Baseline SARS-CoV-2 status positive: Positive RT-PCR test for SARS-CoV-2 OR a positive serology test based on Elecsys immunoassay specific to SARS-CoV-2 nucleocapsid at baseline.
[b] Baseline SARS-CoV-2 status negative: Negative RT-PCR test for SARS-CoV-2 AND a negative serology test based on Elecsys immunoassay specific to SARS-CoV-2 nucleocapsid at baseline.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Moderna COVID-19 Vaccine (2024-2025 Formula) is supplied as follows:

NDC 80777-291-80	Carton of 10 single dose pre-filled syringes, each syringe containing 1 dose of 0.25 mL (NDC 80777-291-09)
NDC 80777-291-81	Carton of 10 single dose pre-filled syringes, each syringe containing 1 dose of 0.25 mL (NDC 80777-291-09). Each carton contains 5 blisters, and each blister contains two syringes. Use one syringe per dose.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Storage

Store frozen between -50°C to -15°C (-58°F to 5°F).

After thawing, Moderna COVID-19 Vaccine may be stored refrigerated between 2°C to 8°C (36°F to 46°F) for up to 60 days or up to the expiration date printed on the carton, whichever comes first.

After thawing, Moderna COVID-19 Vaccine may be stored between 8°C to 25°C (46°F to 77°F) for up to 12 hours.

Do not refreeze once thawed.

Thawed syringes can be handled in room light conditions.

Transportation of Thawed Syringes at 2°C to 8°C (36°F to 46°F)

Thawed pre-filled syringes can be transported at 2°C to 8°C (36°F to 46°F) in shipping containers qualified to maintain 2°C to 8°C (36°F to 46°F). Once thawed and transported at 2°C to 8°C (36°C to 46°F), pre-filled syringes should not be refrozen and should be stored at 2°C to 8°C (36°F to 46°F) until use.

17 PATIENT COUNSELING INFORMATION

Advise the recipient or caregiver to read the Fact Sheet for Recipients and Caregivers.

The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system. Advise recipient or caregiver that more information about IISs can be found at: https://www.cdc.gov/vaccines/programs/iis/about.html.

18 MANUFACTURER INFORMATION

For general questions, send an email or call the telephone number provided below.

Email	Telephone number
medinfo@modernatx.com	1-866-MODERNA (1-866-663-3762)

This EUA Prescribing Information may have been updated. For the most recent Full EUA Prescribing Information, please visit www.modernatx.com/covid19vaccine-eua.

Moderna US, Inc.
Princeton, NJ 08540

Patent(s): www.modernatx.com/patents
Revised: August 2024

EXHIBIT C

Fact Sheet for Recipients and Caregivers

(Starts on Following Page)

FACT SHEET FOR RECIPIENTS AND CAREGIVERS ABOUT MODERNA COVID-19 VACCINE (2024-2025 FORMULA) WHICH HAS EMERGENCY USE AUTHORIZATION (EUA) TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19) IN INDIVIDUALS 6 MONTHS THROUGH 11 YEARS OF AGE

Your child is being offered Moderna COVID-19 Vaccine (2024-2025 Formula)[1] to prevent coronavirus disease 2019 (COVID-19), which is caused by the virus SARS-CoV-2.[2] This Fact Sheet contains information to help you understand the risks and benefits of Moderna COVID-19 Vaccine (2024-2025 Formula), hereafter referred to as Moderna COVID-19 Vaccine, which your child may receive because there is currently a pandemic of COVID-19. Talk to your child's vaccination provider if you have questions.

This Fact Sheet may have been updated. For the most recent Fact Sheet, please see www.modernatx.com/covid19vaccine-eua.

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to make Moderna COVID-19 Vaccine available during the COVID-19 pandemic (for more details about an EUA please see "**What is an Emergency Use Authorization?**" at the end of this document). Moderna COVID-19 Vaccine is not an FDA-approved vaccine in the United States. Read this Fact Sheet for information about Moderna COVID-19 Vaccine.

WHAT IS COVID-19?

COVID-19 is caused by a coronavirus called SARS-CoV-2. You can get COVID-19 through close contact with another person who has the virus.

It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have had a wide range of symptoms reported, ranging from mild symptoms to severe illness leading to death. 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; diarrhea.

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[1] Moderna COVID-19 Vaccine (2024-2025 Formula) encodes the spike protein of the SARS-CoV-2 Omicron variant KP.2.

[2] If your child is immunocompromised and turning from 11 to 12 years of age during the vaccination series for immunocompromised individuals, you may receive this Fact Sheet because your child is being offered SPIKEVAX (COVID-19 Vaccine, mRNA) (2024-2025 Formula) (hereafter referred to as SPIKEVAX). SPIKEVAX is an FDA-approved vaccine for prevention of COVID-19 in individuals 12 years of age and older that is authorized under EUA to complete the dosing schedule for immunocompromised individuals who turn from 11 years to 12 years of age during the vaccination series. Under the authorized dosing schedule, these individuals receive the Moderna COVID-19 Vaccine before they turn 12 years old, and complete the vaccination series with SPIKEVAX on or after the date the individual turns 12 years old. The dosing schedule is a three-dose series, with each dose one month apart. The information in this Fact Sheet about the Moderna COVID-19 Vaccine, including information about the benefits, risks, and ingredients of that vaccine, also applies to your child's use of SPIKEVAX, except with respect to the dosing schedule and the ages authorized for use.

WHAT IS MODERNA COVID-19 VACCINE?

Moderna COVID-19 Vaccine is a vaccine for use in individuals 6 months through 11 years of age to prevent COVID-19. The FDA has authorized the emergency use of Moderna COVID-19 Vaccine under an EUA.

Moderna COVID-19 Vaccine may not protect everyone.

WHAT SHOULD YOU MENTION TO THE VACCCINATION PROVIDER BEFORE YOUR CHILD GETS MODERNA COVID-19 VACCINE?

Tell the vaccination provider about all of your child's medical conditions, including if your child:

- has any allergies
- has had myocarditis (inflammation of the heart muscle) or pericarditis (inflammation of the lining outside the heart)
- has a fever
- has a bleeding disorder or is on a blood thinner
- is immunocompromised or is on a medicine that affects your child's immune system
- is pregnant
- is breastfeeding
- has received another COVID-19 vaccine
- has ever fainted in association with an injection

HOW IS THE VACCINE GIVEN?

Moderna COVID-19 Vaccine is given as an injection into the muscle.

Individuals 6 months through 4 years of age:

- **Unvaccinated individuals:** Two doses of Moderna COVID-19 Vaccine are administered. The second dose is administered 1 month after the first.
- **Individuals who have received one previous dose of a Moderna COVID-19 vaccine[3]:** A single dose of Moderna COVID-19 Vaccine is administered 1 month after a previous Moderna COVID-19 vaccine.
- **Individuals who have received two or more previous doses of a Moderna COVID-19 vaccine[2]:** A single dose of Moderna COVID-19 Vaccine is administered at least 2 months after the last previous dose of a Moderna COVID-19 vaccine.

Individuals 5 years through 11 years of age:

- A single dose of Moderna COVID-19 Vaccine is administered to individuals who have not received a COVID-19 vaccine (2024-2025 Formula). You must wait at least 2 months since your last dose of any COVID-19 vaccine.

[3] Previous dose refers to a dose with any prior Moderna COVID-19 vaccine that is no longer authorized for use in the United States.

Immunocompromised individuals 6 months through 11 years of age:
Additional doses of Moderna COVID-19 Vaccine may be administered. For more information, talk to your child's healthcare provider.

WHO SHOULD NOT GET MODERNA COVID-19 VACCINE?

Your child should not get Moderna COVID-19 Vaccine if your child had:

- a severe allergic reaction after a previous dose of any Moderna COVID-19 vaccine.
- a severe allergic reaction to any ingredient in these vaccines.

WHAT ARE THE INGREDIENTS IN THIS VACCINE?

Moderna COVID-19 Vaccine contains the following ingredients: messenger ribonucleic acid (mRNA), lipids (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate trihydrate, and sucrose.

HAS THIS VACCINE BEEN USED BEFORE?

Millions of individuals 6 months of age and older have received a Moderna COVID-19 vaccine under EUA. In clinical trials, approximately 5,000 individuals 6 months through 5 years of age, 4,000 individuals 6 years through 11 years of age, and 30,000 individuals 12 years of age and older have received at least 1 dose of Moderna COVID-19 Vaccine (Original monovalent).[4]

WHAT ARE THE BENEFITS OF MODERNA COVID-19 VACCINE?

FDA has authorized Moderna COVID-19 Vaccine to provide protection against COVID-19.

The duration of protection against COVID-19 is currently unknown.

WHAT ARE THE RISKS OF MODERNA COVID-19 VACCINE?

There is a remote chance that the vaccine could cause a severe allergic reaction. A severe allergic reaction would usually occur within a few minutes to one hour after getting a dose. For this reason, the vaccination provider may ask your child to stay at the place where your child received the vaccine for monitoring after vaccination. Signs of a severe allergic reaction can include:

- Difficulty breathing
- Swelling of the face and throat
- A fast heartbeat
- A bad rash all over the body
- Dizziness and weakness

Myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have occurred in some people who have received mRNA COVID-19 vaccines. Myocarditis and pericarditis following Moderna COVID-19 vaccines have occurred most commonly in young adult males 18 years through 24 years of age. In most of these individuals, symptoms began within a few days following vaccination. The chance of having this occur is very

[4] Moderna COVID-19 Vaccine (Original monovalent) refers to Moderna COVID-19 Vaccine that encodes the spike protein of only the Original SARS-CoV-2. This vaccine is no longer authorized for use in the United States.

low. You should seek medical attention right away if your child has any of the following symptoms after receiving the vaccine, particularly during the 2 weeks after your child receives a dose of the vaccine:

- Chest pain
- Shortness of breath or difficulty breathing
- Feelings of having a fast-beating, fluttering, or pounding heart

Additional symptoms, particularly in children, may include:

- Fainting
- Unusual and persistent irritability
- Unusual and persistent poor feeding
- Unusual and persistent fatigue or lack of energy
- Persistent vomiting
- Persistent pain in the abdomen
- Unusual and persistent cool, pale skin

Side effects that have been reported in clinical trials with Moderna COVID-19 vaccines include:

- Injection site reactions: pain, tenderness and swelling of the lymph nodes in the same arm of the injection or in the groin, swelling (hardness), and redness
- General side effects: fatigue, headache, muscle pain, joint pain, chills, nausea and vomiting, fever, rash, irritability/crying, sleepiness, and loss of appetite

Side effects that have been reported during post-authorization use include:

- Severe allergic reactions
- Urticaria (itchy rash/hives)
- Myocarditis (inflammation of the heart muscle)
- Pericarditis (inflammation of the lining outside the heart)
- Fainting in association with injection of the vaccine
- Febrile seizures (convulsions during a fever)

These may not be all the possible side effects. Serious and unexpected side effects may occur. The possible side effects are still being studied.

WHAT SHOULD I DO ABOUT SIDE EFFECTS?

If your child experiences a severe allergic reaction, call 9-1-1, or go to the nearest hospital.

Call the vaccination provider or your child's healthcare provider if your child has any side effects that bother your child or do not go away.

Report vaccine side effects to FDA/CDC Vaccine Adverse Event Reporting System (VAERS). The VAERS toll-free number is 1-800-822-7967 or report online to https://vaers.hhs.gov/reportevent.html. Please include "Moderna COVID-19 Vaccine (2024-2025 Formula) EUA" in the first line of box #18 of the report form.

In addition, you can report side effects to ModernaTX, Inc. at 1-866-MODERNA (1-866-663-3762).

WHAT IF I DECIDE NOT TO HAVE MY CHILD GET MODERNA COVID-19 VACCINE?
Under the EUA, there is an option to accept or refuse receiving this vaccine. Should you decide for your child not to receive this vaccine, it will not change the standard medical care.

ARE THERE OTHER VACCINES FOR PREVENTING COVID-19 BESIDES MODERNA COVID-19 VACCINE?
Other vaccines to prevent COVID-19 may be available under EUA, including vaccines that encode the spike protein of the SARS-CoV-2 Omicron variant lineage KP.2 (Omicron KP.2).

CAN MY CHILD RECEIVE MODERNA COVID-19 VACCINE AT THE SAME TIME AS OTHER VACCINES?
If you are considering having your child receive Moderna COVID-19 Vaccine with other vaccines, discuss your options with your child's healthcare provider.

WHAT IF MY CHILD IS IMMUNOCOMPROMISED?
Immunocompromised individuals 6 months through 11 years of age may receive additional doses of Moderna COVID-19 Vaccine (see **HOW IS THE VACCINE GIVEN?** above).

Vaccinations may not provide full immunity to COVID-19 in people who are immunocompromised; therefore, your child should continue to maintain physical precautions to help prevent COVID-19. Your child's close contacts should be vaccinated as appropriate.

WHAT ABOUT PREGNANCY OR BREASTFEEDING?
If your child is pregnant or breastfeeding, discuss the options with your child's healthcare provider.

WILL THIS VACCINE GIVE MY CHILD COVID-19?
No. This vaccine does not contain SARS-CoV-2 and cannot give your child COVID-19.

ADDITIONAL INFORMATION
If you have questions, visit the website or call the telephone number provided below.

To access the most recent Fact Sheets, please scan the QR code provided below.

Moderna COVID-19 Vaccine website	Telephone number
www.modernatx.com/covid19vaccine-eua	1-866-MODERNA (1-866-663-3762)

HOW CAN I LEARN MORE?

- Ask the vaccination provider
- Visit CDC at https://www.cdc.gov/coronavirus/2019-ncov/index.html
- Visit FDA at https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization
- Contact your state or local public health department

WHERE WILL VACCINATION INFORMATION BE RECORDED?

The vaccination provider may include your child's vaccination information in your state/local jurisdiction's Immunization Information System (IIS) or other designated system. For more information about IISs, visit: https://www.cdc.gov/vaccines/programs/iis/about.html.

WHAT IS THE COUNTERMEASURES INJURY COMPENSATION PROGRAM?

The Countermeasures Injury Compensation Program (CICP) is a federal program that may help pay for costs of medical care and other specific expenses of certain people who have been seriously injured by certain medicines or vaccines, including this vaccine. Generally, a claim must be submitted to the CICP within one (1) year from the date of receiving the vaccine. To learn more about this program, visit www.hrsa.gov/cicp/ or call 1-855-266-2427.

WHAT IS AN EMERGENCY USE AUTHORIZATION (EUA)?

The FDA has made Moderna COVID-19 Vaccine available under an emergency access mechanism call an EUA. An EUA is supported by a Secretary of Health and Human Services (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic. A product authorized for emergency use has not undergone the same type of review by FDA as an FDA-approved product.

FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, and available alternatives. In addition, the FDA decision is based on the totality of the scientific evidence available showing that the product may be effective to prevent COVID-19 during the COVID-19 pandemic and that the known and potential benefits of the product outweigh the known and potential risks of the product. All of these criteria must be met to allow for the product to be used under EUA during the COVID-19 pandemic.

The EUA is in effect for the duration of the COVID-19 EUA declaration justifying emergency use of this product, unless terminated or revoked (after which the product may no longer be used under the EUA).

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Princeton, NJ 08540

Patent(s): www.modernatx.com/patents
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Scan to capture that this Fact Sheet was provided to vaccine recipient for the electronic medical records/immunization information systems.

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