FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE: EMERGENCY USE AUTHORIZATION OF MODERNA COVID-19 VACCINE, BIVALENT (ORIGINAL AND OMICRON BA.4/BA.5)

HIGHLIGHTS OF EMERGENCY USE AUTHORIZATION (EUA)
These highlights of the EUA do not include all the information needed to use Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) under the EUA. See the FULL FACT SHEET FOR HEALTHCARE PROVIDERS for Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5).

Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)
Suspension for injection, for intramuscular use
Original EUA Authorized Date: 12/2020
Most Recent EUA Authorized Date: 4/2023

----------RECENT MAJOR CHANGES----------
Dosage and Administration, Dose and Schedule (2.3) 4/2023

----------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, Bivalent (Original and Omicron BA.4/BA.5) 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 of age and older. Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) is not licensed for any use.

See Full Fact Sheet for Healthcare Providers for the justification for emergency use of Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5), information on available alternatives, and additional information on COVID-19.

----------DOSAGE AND ADMINISTRATION----------
For intramuscular injection only. (2)

Individuals 6 Months of Age and Older Not Previously Vaccinated with a COVID-19 Vaccine (2.3)

Age	Moderna COVID-19 Vaccine, Bivalent Vial Cap and Label Color	Dosing Regimen, Dose, and Schedule
6m-5y	Dark Blue Cap and a Label with Gray Border	2 doses, 0.25 mL each Dose 1: month 0 Dose 2: month 1
6-11y	Dark Blue Cap and a Label with Gray Border	Single dose, 0.25 mL
12-64y	Dark Blue Cap and a Label with Gray Border	Single dose, 0.5 mL
≥65y	Dark Blue Cap and a Label with Gray Border	Single dose, 0.5 mL One additional dose, 0.5 mL, may be administered ≥4 months after first dose of an authorized bivalent COVID-19 vaccine

Individuals 6 Months Through 5 Years of Age Previously Vaccinated with Moderna COVID-19 Vaccine[1] (2.3)

Age	Number of Previous Doses of Moderna COVID-19 Vaccine	Moderna COVID-19 Vaccine, Bivalent Vial Cap and Label Color	Dosing Regimen, Dose and Schedule
6m-5y	1 previous dose	Dark Blue Cap and a Label with Gray Border	Single Dose, 0.25 mL One month after receipt of Moderna COVID-19 Vaccine
6m-5y[2]	2 previous doses	Dark Pink Cap and a Label with a Yellow Box	Single dose, 0.2 mL ≥2 months after receipt of Moderna COVID-19 Vaccine

[1] The monovalent Moderna COVID-19 Vaccine is no longer authorized for use in the United States.
[2] For individuals with certain kinds of immunocompromise (as defined in footnote 4), see text below tables for dosing regimen, dose and schedule

Individuals 6 Years of Age and Older Previously Vaccinated with 1 or More Doses of Any Monovalent COVID-19 Vaccine[3] (2.3)

Age	Moderna COVID-19 Vaccine, Bivalent Vial Cap and Label Color	Dosing Regimen, Dose and Schedule
6-11y	Dark Blue Cap and a Label with Gray Border	Single dose, 0.25 mL ≥2 months after monovalent COVID-19 vaccine
12-64y	Dark Blue Cap and a Label with Gray Border	Single dose, 0.5 mL ≥2 months after monovalent COVID-19 vaccine
≥65y	Dark Blue Cap and a Label with Gray Border	Single dose, 0.5 mL ≥2 months after monovalent COVID-19 vaccine One additional dose, 0.5 mL, may be administered ≥4 months after first dose of an authorized bivalent COVID-19 vaccine

[3] Monovalent refers to any COVID-19 vaccine that contains or encodes the spike protein of only the Original SARS-CoV-2.

For individuals with certain kinds of immunocompromise[4] 6 months through 5 years of age who have received two 0.25 mL doses (Moderna COVID-19 Vaccine or Moderna COVID-19 Vaccine, Bivalent), an additional 0.25 mL dose of Moderna COVID-19 Vaccine, Bivalent (vial with a dark blue cap and a label with a gray border) may be administered at least 1 month following the most recent dose; additional doses of Moderna COVID-19 Vaccine, Bivalent[5] may be administered at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.

For individuals with certain kinds of immunocompromise[4] 6 years of age and older, a single additional age-appropriate dose of Moderna COVID-19 Vaccine, Bivalent may be administered at

least 2 months following the initial dose of a bivalent COVID-19 vaccine; additional age-appropriate doses of Moderna COVID-19 Vaccine, Bivalent may be administered at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.

[4] 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.
[5] Providers may use either a 0.25 mL dose from the presentation with a dark blue cap and a label with a gray border or a 0.2 mL dose from the presentation with a dark pink cap and a label with a yellow box.

----------DOSAGE FORMS AND STRENGTHS----------
Moderna COVID-19 Vaccine, Bivalent is a suspension for injection.

Individuals 6 months through 5 years: A single dose is 0.25 mL or 0.2 mL, depending on dose number.

Individuals 6 years through 11 years of age: A single dose is 0.25 mL.

Individuals 12 years of age and older: A single dose is 0.5 mL. (3)

----------CONTRAINDICATIONS----------
Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of Moderna COVID-19 Vaccine or Moderna COVID-19 Vaccine, Bivalent. (4)

----------WARNINGS AND PRECAUTIONS----------
Postmarketing data with authorized or approved monovalent 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 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 of age and older:** Injection site erythema, pain and swelling; arthralgia, axillary (or groin) swelling/tenderness, chills, fatigue, fever, headache, myalgia, nausea/vomiting, and rash. (6.1)

Vaccination providers enrolled in the federal COVID-19 Vaccination Program must report all vaccine administration errors, all serious adverse events, cases of myocarditis, cases of pericarditis, cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and cases of COVID-19 that result in hospitalization or death following administration of Moderna COVID-19 Vaccine, Bivalent 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-MODERNA (1-866-663-3762) or provide a copy of the VAERS form to ModernaTX, Inc. (https://report.moderna.convergehealthsafety.com/) (6.3)

See FACT SHEET FOR RECIPIENTS AND CAREGIVERS

TABLE OF CONTENTS*

* Sections or subsections omitted from the EUA are not listed

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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, Bivalent (Original and Omicron BA.4/BA.5) 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 of age and older.

Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) is hereafter referred to as Moderna COVID-19 Vaccine, Bivalent.

Moderna COVID-19 Vaccine, Bivalent is not licensed for any use.

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

[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.").

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:
    - 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

There may be clinical trials or availability under EUA of other COVID-19 vaccines, including bivalent vaccines that contain or encode the spike protein of the Omicron variant of SARS-CoV-2. SPIKEVAX (COVID-19 Vaccine, mRNA) and COMIRNATY (COVID-19 Vaccine, mRNA) are FDA-approved monovalent COVID-19 vaccines.

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

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Preparation for Administration

- Moderna COVID-19 Vaccine, Bivalent multiple-dose vials contain a frozen suspension that does not contain a preservative and must be thawed prior to administration.
- There are 2 presentations of Moderna COVID-19 Vaccine, Bivalent:
    - Multiple-Dose Vials with Dark Blue Caps and Labels with a Gray Border. The cartons and vial labels state "BOOSTER DOSES ONLY." This presentation is authorized to provide doses for individuals 6 months of age and older. *[See Dose and Schedule (2.3)]*
    - Multiple-Dose Vials with Dark Pink Caps and Labels with a Yellow Box. The cartons and vial labels state "BOOSTER DOSES ONLY." This presentation is authorized to provide certain doses for individuals 6 months through 5 years of age. *[See Dose and Schedule (2.3)]*
- Thaw each vial before use following the instructions below.

Thawing Instructions for Moderna COVID-19 Vaccine, Bivalent Multiple-Dose Vials with Dark Blue Caps and Labels with a Gray Border

Thaw in Refrigerator	Thaw at Room Temperature
Thaw between 2°C to 8°C (36°F to 46°F) for 2 hours. Let each vial stand at room temperature for 15 minutes before administering.	Alternatively, thaw between 15°C to 25°C (59°F to 77°F) for 45 minutes.

Thawing Instructions for Moderna COVID-19 Vaccine, Bivalent Multiple-Dose Vials with Dark Pink Caps and Labels with a Yellow Box

Thaw in Refrigerator	Thaw at Room Temperature
Thaw between 2°C to 8°C (36°F to 46°F) for 45 minutes. Let each vial stand at room temperature for 15 minutes before administering.	Alternatively, thaw between 15°C to 25°C (59°F to 77°F) for 15 minutes.

- After thawing, do not refreeze.
- Swirl vial gently after thawing and between each withdrawal. **Do not shake.** Do not dilute the vaccine.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
- Moderna COVID-19 Vaccine, Bivalent 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.
- Each multiple-dose vial with a dark pink cap and a yellow box contains 2 doses of 0.2 mL.
- For multiple-dose vials with a dark blue cap and label with a gray border, both 0.5 mL doses and 0.25 mL doses may be withdrawn from the same vial. If withdrawing only 0.5 mL doses, each multiple-dose vial with a dark blue cap and label with a gray border contains 5 doses. If withdrawing only 0.25 mL doses, each multiple-dose vial with a dark blue cap and label with a gray border contains 10 doses.
- If the amount of vaccine remaining in the vial cannot provide a full dose appropriate for the individual being vaccinated, discard the vial and contents. Do not pool excess vaccine from multiple vials.
- After the first dose has been withdrawn, the vial should be held between 2°C to 25°C (36°F to 77°F). Record the date and time of first use on the Moderna COVID-19 Vaccine, Bivalent vial label. Discard multiple-dose vials with dark blue caps and labels with a gray border after 12 hours. Discard multiple-dose vials with dark pink caps and labels with a yellow box after 8 hours. Do not refreeze.

2.2 Administration

Administer Moderna COVID-19 Vaccine, Bivalent intramuscularly.

2.3 Dose and Schedule

Individuals 6 Months of Age and Older Not Previously Vaccinated with Any COVID-19 Vaccine

Age	Moderna COVID-19 Vaccine, Bivalent Vial Cap and Label Color	Dosing Regimen, Dose, and Schedule
6m-5y	Dark Blue Cap and a Label with Gray Border	2 doses, 0.25 mL each Dose 1: month 0 Dose 2: month 1
6-11y	Dark Blue Cap and a Label with Gray Border	Single dose, 0.25 mL
12-64y	Dark Blue Cap and a Label with Gray Border	Single dose, 0.5 mL
≥65y	Dark Blue Cap and a Label with Gray Border	Single dose, 0.5 mL One additional dose, 0.5 mL, may be administered ≥4 months after first dose of an authorized bivalent COVID-19 vaccine

Individuals 6 Months Through 5 Years of Age Previously Vaccinated with Moderna COVID-19 Vaccine[3]

Age	Number of Previous Doses of Moderna COVID-19 Vaccine	Moderna COVID-19 Vaccine, Bivalent Vial Cap and Label Color	Dosing Regimen, Dose and Schedule
6m-5y	1 previous dose	Dark Blue Cap and a Label with Gray Border	Single Dose, 0.25 mL One month after receipt of Moderna COVID-19 Vaccine
6m-5y[4]	2 previous doses	Dark Pink Cap and a Label with a Yellow Box	Single dose, 0.2 mL ≥2 months after receipt of Moderna COVID-19 Vaccine

[3] The monovalent Moderna COVID-19 Vaccine is no longer authorized for use in the United States.
[4] For individuals with certain kinds of immunocompromise (as defined in footnote 6), see text below tables for dosing regimen, dose and schedule.

Individuals 6 Years of Age and Older Previously Vaccinated with 1 or More Doses of Any Monovalent COVID-19 Vaccine[5]

Age	Moderna COVID-19 Vaccine, Bivalent Vial Cap and Label Color	Dosing Regimen, Dose and Schedule
6-11y	Dark Blue Cap and a Label with Gray Border	Single dose, 0.25 mL ≥2 months after monovalent COVID-19 vaccine
12-64y	Dark Blue Cap and a Label with Gray Border	Single dose, 0.5 mL ≥2 months after monovalent COVID-19 vaccine
≥65y	Dark Blue Cap and a Label with Gray Border	Single dose, 0.5 mL ≥2 months after monovalent COVID-19 vaccine One additional dose, 0.5 mL, may be administered ≥4 months after first dose of an authorized bivalent COVID-19 vaccine

Individuals with Certain Kinds of Immunocompromise

For individuals with certain kinds of immunocompromise[6] 6 months through 5 years of age who have received two 0.25 mL doses (Moderna COVID-19 Vaccine or Moderna COVID-19 Vaccine, Bivalent), an additional 0.25 mL dose of Moderna COVID-19 Vaccine, Bivalent (vial with a dark blue cap and a label with a gray border) may be administered at least 1 month following the most recent dose; additional doses of Moderna COVID-19 Vaccine, Bivalent[7] may be administered at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.

For individuals with certain kinds of immunocompromise[6] 6 years of age and older, a single additional age-appropriate dose of Moderna COVID-19 Vaccine, Bivalent may be administered at least 2 months following the initial dose of a bivalent COVID-19 vaccine; additional age-appropriate doses of Moderna COVID-19 Vaccine, Bivalent may be administered at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.

3 DOSAGE FORMS AND STRENGTHS

Moderna COVID-19 Vaccine, Bivalent, is a suspension for injection.

[5] Monovalent refers to any COVID-19 vaccine that contains or encodes the spike protein of only the Original SARS-CoV-2.
[6] 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.
[7] Providers may use either a 0.25 mL dose from the presentation with a dark blue cap and a label with a gray border or a 0.2 mL dose from the presentation with a dark pink cap and a label with a yellow box.

Individuals 6 months through 5 years: A single dose is 0.25 mL or 0.2 mL, depending on dose number.

Individuals 6 years through 11 years of age: A single dose is 0.25 mL.

Individuals 12 years of age and older: A single dose is 0.5 mL.

4 CONTRAINDICATIONS

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

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of Moderna COVID-19 Vaccine, Bivalent.

Monitor Moderna COVID-19 Vaccine, Bivalent 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 safety data with Moderna COVID-19 Vaccine are relevant to Moderna COVID-19 Vaccine, Bivalent because these vaccines are manufactured using the same process.

Postmarketing data with authorized or approved monovalent 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 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, Bivalent.

5.5 Limitations of Vaccine Effectiveness

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

6 ADVERSE REACTIONS

The safety data accrued with Moderna COVID-19 Vaccine (no longer authorized for use in the U.S.) and 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)] are relevant to Moderna COVID-19 Vaccine, Bivalent because these vaccines are manufactured using the same process.

The safety of Moderna COVID-19 Vaccine, Bivalent in individuals 6 months of age and older is based on:

- safety data from clinical trials which evaluated primary and booster vaccination with Moderna COVID-19 Vaccine,
- safety data from a clinical study which evaluated a booster dose of bivalent vaccine (Original and Omicron BA.1), and
- postmarketing safety data with Moderna COVID-19 Vaccine and Moderna COVID-19 Vaccine, Bivalent.

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.

In five clinical trials (NCT04283461, NCT04405076, NCT04470427, NCT04649151, NCT04796896), approximately 40,000 participants aged 6 months and older received at least one dose of Moderna COVID-19 Vaccine. In one clinical trial (NCT04927065), approximately 400 participants 18 years of age and older received one dose of bivalent vaccine (Original and Omicron BA.1).

Study 1 (NCT04470427) is a Phase 3 randomized, placebo-controlled, observer-blind clinical trial 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[8] (100 mcg messenger RNA [mRNA]; n=15,184) or placebo (n=15,162). Study 2 (NCT04405076) is a Phase 2, randomized, observer-blind, placebo-controlled, dose-confirmation study, which included an open-label phase

[8] Moderna COVID-19 Vaccine is marketed as SPIKEVAX (COVID-19 Vaccine, mRNA), which is approved for use in individuals 18 years of age and older.

involving 171 participants 18 years of age and older who received a booster dose of Moderna COVID-19 Vaccine (50 mcg mRNA) 6 months (range of 5.8 to 8.5 months) after receiving the second dose of the primary series. Study 3 (NCT04649151) is a Phase 2/3 clinical trial with multiple parts. The first portion of the trial was a randomized, placebo-controlled, observer-blind trial 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). The trial transitioned to an open-label study in which 1,364 participants 12 years through 17 years of age received a booster dose of Moderna COVID-19 Vaccine (50 mcg mRNA) at least 5 months after the second dose of the primary series. Study 4 (NCT04796896) is a Phase 2/3 clinical trial with multiple parts. The study includes a randomized, placebo-controlled, observer-blind clinical trial component conducted in the United States and Canada involving 10,390 participants 6 months through 11 years of age who received at least one dose of Moderna COVID-19 Vaccine (25 mcg mRNA for ages 6 months through 5 years and 50 mcg mRNA for ages 6 years through 11 years; n=7,799) or placebo (n=2,591). The trial protocol was amended to include an open-label booster dose phase which included 145 participants 17 months through 5 years of age and 1,294 participants 6 years through 11 years of age who received a booster dose of Moderna COVID-19 Vaccine (10 mcg mRNA and 25 mcg mRNA, respectively) at least 6 months after completion of the Moderna COVID-19 Vaccine two-dose primary series. Study 5 (NCT04927065) is Phase 2/3 open-label study in which 437 participants 18 years of age and older, who had 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) (50 mcg mRNA) at least 3 months after the first booster dose.

Moderna COVID-19 Vaccine Administered as a Two-Dose Primary Series

Participants 18 Years of Age and Older

The safety of Moderna COVID-19 Vaccine was evaluated in an ongoing Phase 3 randomized, placebo-controlled, observer-blind clinical trial 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); 22,826 (75.2%) participants were 18 to 64 years of age and 7,520 (24.8%) participants 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.

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=15,179) and participants receiving placebo (n=15,159) with at least 1 documented dose. Events that persisted for more than 7 days were followed until resolution. Solicited adverse reactions were reported more frequently among vaccine participants than placebo participants.

The reported number and percentage of the solicited local and systemic adverse reactions by age group and dose are presented in Table 1 and Table 2, respectively.

Table 1: Number and Percentage of Participants With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After Each Dose in Participants 18 Years Through 64 Years (Solicited Safety Set, Dose 1 and Dose 2)†

	Moderna COVID-19 Vaccine		**Placebo[a]**	
	Dose 1 (N=11,406) n (%)	**Dose 2** (N=11,000) n (%)	**Dose 1** (N=11,402) n (%)	**Dose 2** (N=10,929) n (%)
Local Adverse Reactions				
Pain	9,908 (86.9)	9,893 (89.9)	2,183 (19.1)	2,048 (18.7)
Pain, Grade 3[b]	366 (3.2)	506 (4.6)	23 (0.2)	22 (0.2)
Axillary swelling/tenderness	1,322 (11.6)	1,777 (16.2)	567 (5.0)	474 (4.3)
Axillary swelling/tenderness, Grade 3[b]	37 (0.3)	47 (0.4)	13 (0.1)	12 (0.1)
Swelling (hardness) ≥25 mm	766 (6.7)	1,399 (12.7)	42 (0.4)	46 (0.4)
Swelling (hardness), Grade 3[c]	62 (0.5)	183 (1.7)	3 (<0.1)	5 (<0.1)
Erythema (redness) ≥25 mm	354 (3.1)	989 (9.0)	54 (0.5)	53 (0.5)
Erythema (redness), Grade 3[c]	34 (0.3)	210 (1.9)	11 (<0.1)	12 (0.1)
Systemic Adverse Reactions				
Fatigue	4,385 (38.5)	7,453 (67.8)	3,281 (28.8)	2,701 (24.7)
Fatigue, Grade 3[d]	121 (1.1)	1,178 (10.7)	83 (0.7)	88 (0.8)
Fatigue, Grade 4[e]	1 (<0.1)	0 (0)	0 (0)	0 (0)
Headache	4,028 (35.3)	6,929 (63.0)	3,303 (29.0)	2,775 (25.4)
Headache, Grade 3[f]	220 (1.9)	559 (5.1)	163 (1.4)	132 (1.2)

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=11,406) n (%)	**Dose 2** (N=11,000) n (%)	**Dose 1** (N=11,402) n (%)	**Dose 2** (N=10,929) n (%)
Myalgia	2,700 (23.7)	6,789 (61.7)	1,625 (14.3)	1,425 (13.0)
Myalgia, Grade 3[d]	74 (0.6)	1,116 (10.1)	38 (0.3)	42 (0.4)
Arthralgia	1,892 (16.6)	5,010 (45.6)	1,327 (11.6)	1,180 (10.8)
Arthralgia, Grade 3[d]	47 (0.4)	650 (5.9)	30 (0.3)	37 (0.3)
Arthralgia, Grade 4[e]	1 (<0.1)	0 (0)	0 (0)	0 (0)
Chills	1,050 (9.2)	5,357 (48.7)	730 (6.4)	662 (6.1)
Chills, Grade 3[g]	17 (0.1)	164 (1.5)	8 (<0.1)	15 (0.1)
Nausea/vomiting	1,068 (9.4)	2,355 (21.4)	908 (8.0)	807 (7.4)
Nausea/vomiting, Grade 3[h]	6 (<0.1)	11 (0.1)	8 (<0.1)	8 (<0.1)
Fever	102 (0.9)	1,909 (17.4)	37 (0.3)	38 (0.3)
Fever, Grade 3[i]	10 (<0.1)	185 (1.7)	1 (<0.1)	2 (<0.1)
Fever, Grade 4[j]	4 (<0.1)	12 (0.1)	4 (<0.1)	2 (<0.1)
Use of antipyretic or pain medication	2,656 (23.3)	6,307 (57.3)	1,523 (13.4)	1,254 (11.5)

* 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] Placebo was a saline solution.

[b] Grade 3 pain and axillary swelling/tenderness: Defined as any use of prescription pain reliever; prevents daily activity.

[c] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.

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

[e] Grade 4 fatigue, arthralgia: Defined as requires emergency room visit or hospitalization.

[f] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.

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

[h] Grade 3 nausea/vomiting: Defined as prevents daily activity; requires outpatient intravenous hydration.

[i] Grade 3 fever: Defined as ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F.

[j] Grade 4 fever: Defined as >40.0°C / >104.0°F.

Table 2: Number and Percentage of Participants With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After Each Dose in Participants 65 Years and Older (Solicited Safety Set, Dose 1 and Dose 2)†

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=3,760) n (%)	**Dose 2** (N=3,691) n (%)	**Dose 1** (N=3,749) n (%)	**Dose 2** (N=3,649) n (%)
Local Adverse Reactions				
Pain	2,780 (73.9)	3,071 (83.2)	482 (12.9)	438 (12.0)
Pain, Grade 3[b]	50 (1.3)	100 (2.7)	32 (0.9)	19 (0.5)
Axillary swelling/tenderness	231 (6.1)	315 (8.5)	155 (4.1)	97 (2.7)
Axillary swelling/tenderness, Grade 3[b]	12 (0.3)	21 (0.6)	14 (0.4)	8 (0.2)
Swelling (hardness) ≥25 mm	169 (4.5)	408 (11.1)	23 (0.6)	14 (0.4)
Swelling (hardness), Grade 3[c]	20 (0.5)	72 (2.0)	3 (<0.1)	7 (0.2)
Erythema (redness) ≥25 mm	91 (2.4)	285 (7.7)	23 (0.6)	15 (0.4)
Erythema (redness), Grade 3[c]	8 (0.2)	77 (2.1)	2 (<0.1)	3 (<0.1)
Systemic Adverse Reactions				
Fatigue	1,251 (33.3)	2,154 (58.4)	852 (22.7)	717 (19.6)
Fatigue, Grade 3[d]	30 (0.8)	255 (6.9)	22 (0.6)	20 (0.5)
Headache	922 (24.5)	1,708 (46.3)	723 (19.3)	652 (17.9)
Headache, Grade 3[e]	53 (1.4)	107 (2.9)	34 (0.9)	33 (0.9)
Myalgia	742 (19.7)	1,740 (47.2)	444 (11.9)	399 (10.9)
Myalgia, Grade 3[d]	17 (0.5)	205 (5.6)	9 (0.2)	10 (0.3)
Arthralgia	618 (16.4)	1,293 (35.1)	457 (12.2)	399 (10.9)
Arthralgia, Grade 3[d]	13 (0.3)	125 (3.4)	8 (0.2)	7 (0.2)
Chills	201 (5.3)	1,143 (31.0)	148 (4.0)	151 (4.1)
Chills, Grade 3[f]	7 (0.2)	27 (0.7)	6 (0.2)	2 (<0.1)
Nausea/vomiting	194 (5.2)	439 (11.9)	167 (4.5)	134 (3.7)
Nausea/vomiting, Grade 3[g]	4 (0.1)	10 (0.3)	5 (0.1)	3 (<0.1)

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=3,760) n (%)	**Dose 2** (N=3,691) n (%)	**Dose 1** (N=3,749) n (%)	**Dose 2** (N=3,649) n (%)
Nausea/vomiting, Grade 4[h]	0 (0)	1 (<0.1)	0 (0)	0 (0)
Fever	10 (0.3)	367 (9.9)	7 (0.2)	5 (0.1)
Fever, Grade 3[i]	1 (<0.1)	18 (0.5)	1 (<0.1)	0 (0)
Fever, Grade 4[j]	0 (0)	1 (<0.1)	2 (<0.1)	1 (<0.1)
Use of antipyretic or pain medication	673 (17.9)	1,548 (41.9)	477 (12.7)	331 (9.1)

* 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] Placebo was a saline solution.
[b] Grade 3 pain and axillary swelling/tenderness: Defined as any use of prescription pain reliever; prevents daily activity.
[c] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.
[d] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
[e] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
[f] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
[g] Grade 3 nausea/vomiting: Defined as prevents daily activity; requires outpatient intravenous hydration.
[h] Grade 4 nausea/vomiting: Defined as requires emergency room visit or hospitalization for hypotensive shock.
[i] Grade 3 fever: Defined as ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F.
[j] Grade 4 fever: Defined as >40.0°C / >104.0°F.

Solicited local and systemic adverse reactions reported following administration of Moderna COVID-19 Vaccine had a median duration of 1 to 3 days.

Grade 3 solicited local adverse reactions were more frequently reported after Dose 2 than after Dose 1. Solicited systemic adverse reactions were more frequently reported by vaccine recipients after Dose 2 than after Dose 1.

In Study 1, 2.3% of participants (vaccine=347, placebo=337) had evidence of prior SARS-CoV-2 infection at baseline (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]). Overall, among the 347 vaccine participants, there were no notable differences in reactogenicity compared to the 14,750 vaccine participants who had no evidence of prior SARS-CoV-2 infection at baseline (negative RT-PCR test and negative Elecsys immunoassay result at Day 1).

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

Safety data for Moderna COVID-19 Vaccine in adolescents were collected in an ongoing Phase 2/3 clinical trial with multiple parts. The first portion of the trial was a randomized, placebo-controlled, observer-blind, clinical trial 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). Overall, 51.4% were male, 48.6% were female, 11.6% were Hispanic or Latino, 83.9% were White, 3.4% were African American, 5.9% 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.

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=2,485) and participants receiving placebo (n=1,240) 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 12 years through 17 years of age by dose are presented in Table 3.

Table 3: Number and Percentage of Participants With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After Each Dose in Participants 12 Years Through 17 Years (Solicited Safety Set, Dose 1 and Dose 2)†

	Moderna COVID-19 Vaccine		**Placebo[a]**	
	Dose 1 (N=2,482) n (%)	**Dose 2** (N=2,478) n (%)	**Dose 1** (N=1,238) n (%)	**Dose 2** (N=1,220) n (%)
Local Adverse Reactions				
Pain	2,310 (93.1)	2,290 (92.4)	431 (34.8)	370 (30.3)
Pain, Grade 3[b]	133 (5.4)	126 (5.1)	1 (<0.1)	3 (0.2)
Axillary swelling/tenderness	578 (23.3)	519 (21.0)	101 (8.2)	61 (5.0)
Axillary swelling/tenderness, Grade 3[b]	10 (0.4)	7 (0.3)	0 (0)	0 (0)
Swelling (hardness) ≥25 mm	403 (16.2)	509 (20.5)	12 (1.0)	12 (1.0)

	Moderna COVID-19 Vaccine		Placebo[a]	
	Dose 1 (N=2,482) n (%)	**Dose 2** (N=2,478) n (%)	**Dose 1** (N=1,238) n (%)	**Dose 2** (N=1,220) n (%)
Swelling (hardness), Grade 3[c]	27 (1.1)	56 (2.3)	0 (0)	0 (0)
Erythema (redness) ≥25 mm	334 (13.5)	484 (19.5)	8 (0.6)	11 (0.9)
Erythema (redness), Grade 3[c]	21 (0.8)	72 (2.9)	0 (0)	0 (0)
Systemic Adverse Reactions				
Fatigue	1,188 (47.9)	1,679 (67.8)	453 (36.6)	353 (28.9)
Fatigue, Grade 3[d]	33 (1.3)	188 (7.6)	18 (1.5)	10 (0.8)
Headache	1,106 (44.6)	1,739 (70.2)	477 (38.5)	370 (30.3)
Headache, Grade 3[e]	56 (2.3)	112 (4.5)	17 (1.4)	14 (1.1)
Headache, Grade 4[f]	0 (0)	1 (<0.1)	0 (0)	0 (0)
Myalgia	668 (26.9)	1,154 (46.6)	205 (16.6)	153 (12.5)
Myalgia, Grade 3[d]	24 (1.0)	129 (5.2)	10 (0.8)	3 (0.2)
Arthralgia	371 (15.0)	716 (28.9)	143 (11.6)	113 (9.3)
Arthralgia, Grade 3[d]	15 (0.6)	57 (2.3)	5 (0.4)	2 (0.2)
Chills	456 (18.4)	1,066 (43.0)	138 (11.1)	97 (8.0)
Chills, Grade 3[g]	4 (0.2)	11 (0.4)	1 (<0.1)	0 (0)
Nausea/vomiting	281 (11.3)	591 (23.9)	110 (8.9)	106 (8.7)
Nausea/vomiting, Grade 3[h]	2 (<0.1)	2 (<0.1)	0 (0)	0 (0)
Nausea/vomiting, Grade 4[i]	0 (0)	1 (<0.1)	0 (0)	0 (0)
Fever	63 (2.5)	302 (12.2)	12 (1.0)	12 (1.0)
Fever, Grade 3[j]	9 (0.4)	46 (1.9)	1 (<0.1)	1 (<0.1)
Fever, Grade 4[k]	0 (0)	1 (<0.1)	0 (0)	1 (<0.1)
Use of antipyretic or pain medication	748 (30.1)	1,242 (50.1)	118 (9.5)	108 (8.9)

* 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] Placebo was a saline solution.

[b] Grade 3 pain and axillary swelling/tenderness: Defined as any use of prescription pain reliever; prevents daily activity.
[c] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.
[d] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
[e] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
[f] Grade 4 headache: Defined as requires emergency room visit or hospitalization.
[g] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
[h] Grade 3 nausea/vomiting: Defined as prevents daily activity, requires outpatient intravenous hydration.
[i] Grade 4 nausea/vomiting: Defined as requires emergency room visit or hospitalization for hypotensive shock.
[j] Grade 3 fever: Defined as ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F.
[k] Grade 4 fever: Defined as >40.0°C / >104.0°F.

Solicited local and systemic adverse reactions reported following administration of Moderna COVID-19 Vaccine had a median duration of 1 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 12 years through 17 years, 5.8% of participants (vaccine=147, placebo=69) had evidence of prior SARS-CoV-2 infection at baseline. Table 4 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 4: Number and Percentage of Participants 12 Years Through 17 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=147) n (%)	**Dose 2** (N=146) n (%)	**Dose 1** (N=2,163) n (%)	**Dose 2** (N=2,162) n (%)
Local Adverse Reactions				
Pain	128 (87.1)	124 (84.9)	2,023 (93.5)	2,006 (92.8)
Pain, Grade 3[a]	9 (6.1)	7 (4.8)	113 (5.2)	114 (5.3)
Axillary swelling/tenderness	58 (39.5)	25 (17.1)	487 (22.5)	465 (21.5)
Axillary swelling/tenderness, Grade 3[a]	1 (0.7)	0 (0)	9 (0.4)	7 (0.3)
Swelling (hardness) ≥25 mm	24 (16.3)	22 (15.1)	360 (16.6)	449 (20.8)
Swelling (hardness), Grade 3[b]	4 (2.7)	2 (1.4)	21 (1.0)	50 (2.3)
Erythema (redness) ≥25 mm	19 (12.9)	18 (12.3)	308 (14.2)	432 (20.0)

	Baseline SARS-CoV-2 Positive		Baseline SARS-CoV-2 Negative	
	Dose 1 (N=147) n (%)	**Dose 2** (N=146) n (%)	**Dose 1** (N=2,163) n (%)	**Dose 2** (N=2,162) n (%)
Erythema (redness), Grade 3[b]	1 (0.7)	3 (2.1)	19 (0.9)	62 (2.9)
Systemic Adverse Reactions				
Fatigue	103 (70.1)	94 (64.4)	1,004 (46.4)	1,470 (68.0)
Fatigue, Grade 3[c]	4 (2.7)	5 (3.4)	27 (1.2)	173 (8.0)
Headache	103 (70.1)	90 (61.6)	938 (43.4)	1,527 (70.6)
Headache, Grade 3[d]	11 (7.5)	7 (4.8)	44 (2.0)	96 (4.4)
Headache, Grade 4[e]	0 (0)	0 (0)	0 (0)	1 (<0.1)
Myalgia	63 (42.9)	63 (43.2)	557 (25.8)	1,017 (47.1)
Myalgia, Grade 3[c]	3 (2.0)	2 (1.4)	19 (0.9)	117 (5.4)
Arthralgia	36 (24.5)	39 (26.7)	305 (14.1)	633 (29.3)
Arthralgia, Grade 3[c]	2 (1.4)	0 (0)	12 (0.6)	52 (2.4)
Chills	72 (49.0)	63 (43.2)	363 (16.8)	934 (43.2)
Chills, Grade 3[f]	0 (0)	0 (0)	4 (0.2)	10 (0.5)
Nausea/vomiting	30 (20.4)	29 (19.9)	237 (11.0)	522 (24.2)
Nausea/vomiting, Grade 3[g]	0 (0)	0 (0)	2 (<0.1)	2 (<0.1)
Nausea/vomiting, Grade 4[h]	0 (0)	1 (0.7)	0 (0)	0 (0)
Fever	29 (19.7)	20 (13.7)	33 (1.5)	262 (12.1)
Fever, Grade 3[i]	4 (2.7)	2 (1.4)	4 (0.2)	40 (1.9)
Fever, Grade 4[j]	0 (0)	0 (0)	0 (0)	1 (<0.1)

***** 7 days included day of vaccination and the subsequent 6 days. Events 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 and axillary swelling/tenderness: Defined as any use of prescription pain reliever; prevents daily activity.

[b] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.

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

[d] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.

[e] Grade 4 headache: Defined as requires emergency room visit or hospitalization.

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

[g] Grade 3 nausea/vomiting: Defined as prevents daily activity, requires outpatient intravenous hydration.

[h] Grade 4 nausea/vomiting: Defined as requires emergency room visit or hospitalization for hypotensive shock.
[i] Grade 3 fever: Defined as ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F.
[j] Grade 4 fever: Defined as >40.0°C / >104.0°F.

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 May 8, 2021, among participants who had received at least 1 dose of vaccine or placebo (vaccine=2,486, placebo=1,240), unsolicited adverse events that occurred within 28 days following each vaccination were reported by 20.5% of participants (n=510) who received Moderna COVID-19 Vaccine and 15.9% of participants (n=197) who received placebo. In these analyses, 97.3% of study participants had at least 28 days of follow-up after Dose 2.

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. There were no cases of myocarditis among placebo recipients.

During the 28-day follow-up period following any dose, lymphadenopathy-related events that were not necessarily captured in the 7-day e-diary were reported by 5.0% of vaccine recipients and 0.5% 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 adverse events were reported in 1.8% of vaccine recipients and 0.6% 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 0.9% of vaccine recipients and in no 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 that would suggest a causal relationship to Moderna COVID-19 Vaccine.

Serious Adverse Events

As of May 8, 2021, serious adverse events were reported by 0.2% (n=6) of participants who received Moderna COVID-19 Vaccine and 0.2% (n=2) of participants who received placebo. In these analyses, 97.3% of study participants had at least 28 days of follow-up after Dose 2, and the median follow-up time for all participants was 53 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

Study 3 participants started to enter an open-label, observational phase after May 10, 2021. A long-term safety analysis was conducted in participants from Study 3 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 95.6% of study participants have had at least 6 months of follow-up after Dose 2. Through the cut-off date, there were no serious adverse events causally related to the vaccine.

Participants 6 Years Through 11 Years of Age

Safety data for Moderna COVID-19 Vaccine from the blinded portion of Study 4 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 5.

Table 5: 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)

	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 (%)
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)
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 6 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 6: 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)
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)

	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 (%)
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

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 7, participants 24 months through 36 months of age are presented in Table 8, and participants 37 months to 5 years are presented in Table 9.

Table 7: 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)

	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 (%)
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 8: 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)
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 9: 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)
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)

	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 (%)
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 years of age and 2 days for participants 2 years through 5 years of age.

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.

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 Administered as a First Booster Dose Following a Primary Series of Moderna COVID-19 Vaccine

Participants 18 Years of Age and Older

Study 2 is 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 (0.5 mL 1 month apart) of Moderna COVID-19 Vaccine primary series. In an open-label phase, 171 of those participants received a single booster dose (50 mcg mRNA; 0.25 mL) 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); 39.2% were male, 60.8% were female, 5.8% were Hispanic or Latino, 95.9% were White, 2.9% were Black or African American, 0.6% were Asian, and 0.6% were American Indian or Alaska Native. Following the booster dose, the median follow-up time was 5.7 months (range of 3.1 to 6.4 months).

Solicited Adverse Reactions

Table 10 presents the frequency and severity of reported solicited local and systemic adverse reactions among Study 2 Moderna COVID-19 Vaccine booster dose recipients 18 to <65 years of age and ≥65 years of age within 7 days of a booster vaccination.

Table 10: Number and Percentage of Participants 18 Years of Age and Older With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After the Moderna COVID-19 Vaccine Booster Dose (Solicited Safety Set)†

	Participants 18 Years Through 64 Years (N=129) n (%)	**Participants ≥65 Years** (N=38) n (%)
Local Adverse Reactions		
Pain	111 (86.0)	29 (76.3)
Pain, Grade 3[a]	4 (3.1)	2 (5.3)
Axillary swelling/tenderness	32 (24.8)	2 (5.3)
Axillary swelling/tenderness, Grade 3[a]	1 (0.8)	0 (0)
Swelling (hardness) ≥25 mm	8 (6.2)	1 (2.6)
Swelling (hardness), Grade 3[b]	0 (0)	1 (2.6)
Erythema (redness) ≥25 mm	7 (5.4)	1 (2.6)
Erythema (redness), Grade 3[b]	1 (0.8)	0 (0.0)
Systemic Adverse Reactions		
Fatigue	80 (62.0)	18 (47.4)
Fatigue, Grade 3[c]	4 (3.1)	3 (7.9)
Headache	76 (58.9)	16 (42.1)
Headache, Grade 3[d]	1 (0.8)	1 (2.6)
Myalgia	64 (49.6)	18 (47.4)
Myalgia, Grade 3[c]	4 (3.1)	1 (2.6)
Arthralgia	54 (41.9)	15 (39.5)
Arthralgia, Grade 3[c]	4 (3.1)	1 (2.6)
Chills	52 (40.3)	7 (18.4)
Nausea/vomiting	16 (12.4)	3 (7.9)
Fever	9 (7.0)	2 (5.4)
Fever, Grade 3[e]	2 (1.6)	0 (0.0)
Rash	3 (2.3)	0 (0)
Use of antipyretic or pain medication	64 (49.6)	11 (28.9)

* 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] Grade 3 pain and axillary swelling/tenderness: Defined as any use of prescription pain reliever; prevents daily activity.

[b] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.

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

[d] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.

[e] Grade 3 fever: Defined as ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F.

In participants who received a booster dose, the median duration of solicited local and systemic adverse reactions was 2 to 3 days.

Unsolicited Adverse Events

Overall, the 171 participants who received a booster dose had a median follow-up time of 5.7 months after the booster dose to the cut-off date (August 16, 2021). 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

Of the 171 participants who received a booster dose of Moderna COVID-19 Vaccine, there were no serious adverse events reported from the booster dose through 28 days after the booster dose. Through the cut-off date of August 16, 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 2/3 clinical trial with multiple parts. 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 (50 mcg mRNA; 0.25 mL) at least 5 months after the second dose of the primary series (Study 3, NCT04649151). Overall, 51.2% were male, 48.8% were female, 13.1% were Hispanic or Latino, 84.9% were White, 3.2% were African American, 4.8% 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. As of the data cutoff date of May 16, 2022, the median duration of follow-up for safety was 116 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 as a booster dose. Events that persisted for more than 7 days were followed until resolution.

Table 11 presents the frequency and severity of reported solicited local and systemic adverse reactions among Study 3 Moderna COVID-19 Vaccine booster dose recipients 12 years through 17 years of age within 7 days of a booster vaccination.

Table 11: Number and Percentage of Adolescents 12 Years Through 17 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=1,312) n (%)
Local Adverse Reactions	1,196 (91.2)
Pain	1,196 (91.2)
Pain, Grade 3[a]	39 (3.0)
Axillary swelling/tenderness	367 (28.0)
Axillary swelling/tenderness, Grade 3[a]	4 (0.3)
Swelling (hardness) ≥25 mm	176 (13.4)
Swelling (hardness), Grade 3[b]	9 (0.7)
Erythema (redness) ≥25 mm	120 (9.2)
Erythema (redness), Grade 3[b]	9 (0.7)

	Moderna COVID-19 Vaccine Booster Dose (N=1,312) n (%)
Systemic Adverse Reactions	
Fatigue	769 (58.7)
Fatigue, Grade 3[c]	53 (4.0)
Headache	748 (57.1)
Headache, Grade 3[d]	28 (2.1)
Myalgia	529 (40.4)
Myalgia, Grade 3[c]	47 (3.6)
Arthralgia	316 (24.1)
Arthralgia, Grade 3[c]	17 (1.3)
Chills	399 (30.4)
Chills, Grade 3[e]	7 (0.5)
Nausea/vomiting	234 (17.8)
Nausea/vomiting, Grade 3[f]	2 (0.2)
Fever	79 (6.1)
Fever, Grade 3[g]	8 (0.6)
Use of antipyretic or pain medication	515 (39.3)

***** 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 and axillary swelling/tenderness: Defined as any use of prescription pain reliever; prevents daily activity.

[b] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.

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

[d] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.

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

[f] Grade 3 nausea/vomiting: Defined as prevents daily activity; requires outpatient intravenous hydration.

[g] Grade 3 fever: Defined as ≥39.0° – <40.0°C / ≥102.1° – < 104.0°F.

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 16, 2022, among the 1,364 participants who had received a booster dose, unsolicited adverse events that occurred within 28 days following vaccination were reported by 14.2% of participants (n=194). In these analyses, 97.4% of study participants had at least 28 days of follow-up after the booster dose. No new safety concerns were identified.

Serious Adverse Events

Through the cut-off date of May 16, 2022, with a median follow-up duration of 116 days after the booster dose, no serious adverse events following the booster dose were reported.

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 12 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 12: 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)
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)

	Moderna COVID-19 Vaccine Booster Dose (N=1,280) n (%)
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 13, and among participants 37 months through 5 years are presented in Table 14.

Table 13: 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 14: 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 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.

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 bivalent vaccine (Original and Omicron BA.1) and participants receiving Moderna COVID-19 Vaccine. Events that persisted for more than 7 days were followed until resolution.

Table 15 and Table 16 present the frequency and severity of reported solicited local and systemic adverse reactions within 7 days following a second booster dose with bivalent vaccine (Original and Omicron BA.1) booster dose compared to Moderna COVID-19 Vaccine in participants 18 to <65 years of age and ≥65 years of age.

Table 15: Number and Percentage of Participants 18 Years Through 64 Years of Age With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After a Second Booster Dose with Bivalent Vaccine (Original and BA.1) Compared to a Second Booster Dose with Moderna COVID-19 Vaccine (Solicited Safety Set)†

	Bivalent Vaccine (Original and Omicron BA.1) Booster Dose (N=263) n (%)	**Moderna COVID-19 Vaccine Booster Dose** (N=211) n (%)
Local Adverse Reactions		
Pain	231 (87.8)	175 (82.9)
Pain, Grade 3[a]	2 (0.8)	4 (1.9)
Axillary swelling/tenderness	56 (21.3)	39 (18.5)
Axillary swelling/tenderness, Grade 3[a]	0 (0)	4 (1.9)
Swelling (hardness) ≥25 mm	22 (8.4)	15 (7.1)
Swelling (hardness), Grade 3[b]	4 (1.5)	2 (0.9)
Erythema (redness) ≥25 mm	20 (7.6)	10 (4.7)
Erythema (redness), Grade 3[b]	7 (2.7)	1 (0.5)
Systemic Adverse Reactions		
Fatigue	154 (58.6)	115 (54.5)
Fatigue, Grade 3[c]	10 (3.8)	7 (3.3)
Headache	129 (49.0)	100 (47.4)

	Bivalent Vaccine (Original and Omicron BA.1) Booster Dose (N=263) n (%)	Moderna COVID-19 Vaccine Booster Dose (N=211) n (%)
Headache, Grade 3[d]	4 (1.5)	1 (0.5)
Myalgia	113 (43.0)	90 (42.7)
Myalgia, Grade 3[c]	9 (3.4)	8 (3.8)
Arthralgia	87 (33.1)	69 (32.7)
Arthralgia, Grade 3[c]	3 (1.1)	2 (0.9)
Chills	64 (24.3)	54 (25.6)
Chills, Grade 3[e]	1 (0.4)	0 (0)
Nausea/vomiting	35 (13.3)	27 (12.8)
Fever	10 (3.8)	10 (4.7)
Fever, Grade 3[f]	1 (0.4)	0 (0)
Use of antipyretic or pain medication	104 (39.5)	67 (31.8)

* 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). Solicited Safety Set consisted of participants who received a booster dose and contributed solicited adverse reaction data.

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

[a] Grade 3 pain and axillary swelling/tenderness: Defined as any use of prescription pain reliever; prevents daily activity.

[b] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.

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

[d] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.

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

[f] Grade 3 fever: Defined as ≥39.0° – ≤40.0°C / ≥102.1° – ≤104.0°F.

Table 16: Number and Percentage of Participants ≥65 Years of Age With Solicited Local and Systemic Adverse Reactions Starting Within 7 Days* After a Second Booster Dose with Bivalent Vaccine (Original and Omicron BA.1) Compared to a Second Booster Dose with Moderna COVID-19 Vaccine (Solicited Safety Set)†

	Bivalent Vaccine (Original and Omicron BA.1) Booster Dose (N=174) n (%)	Moderna COVID-19 Vaccine Booster Dose (N=140) n (%)
Local Adverse Reactions		
Pain	107 (61.5)	94 (67.1)
Pain, Grade 3[a]	2 (1.1)	0 (0)
Axillary swelling/tenderness	20 (11.5)	15 (10.7)
Axillary swelling/tenderness, Grade 3[a]	1 (0.6)	0 (0)
Swelling (hardness) ≥25 mm	8 (4.6)	8 (5.7)
Swelling (hardness), Grade 3[b]	1 (0.6)	3 (2.1)
Erythema (redness) ≥25 mm	10 (5.7)	3 (2.1)
Erythema (redness), Grade 3[b]	2 (1.1)	1 (0.7)
Systemic Adverse Reactions		
Fatigue	86 (49.4)	65 (46.8)
Fatigue, Grade 3[c]	5 (2.9)	4 (2.9)
Myalgia	60 (34.5)	45 (32.4)
Myalgia, Grade 3[c]	1 (0.6)	5 (3.6)

	Bivalent Vaccine (Original and Omicron BA.1) Booster Dose (N=174) n (%)	**Moderna COVID-19 Vaccine Booster Dose** (N=140) n (%)
Headache	63 (36.2)	44 (31.7)
Headache, Grade 3[d]	1 (0.6)	1 (0.7)
Arthralgia	49 (28.2)	42 (30.2)
Arthralgia, Grade 3[c]	1 (0.6)	1 (0.7)
Chills	40 (23.0)	20 (14.4)
Chills, Grade 3[e]	0 (0)	1 (0.7)
Nausea/vomiting	10 (5.7)	8 (5.8)
Nausea/vomiting, Grade 3[f]	1 (0.6)	0 (0)
Fever	9 (5.2)	2 (1.4)
Use of antipyretic or pain medication	46 (26.4)	40 (28.6)

* 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). Solicited Safety Set consisted of participants who received a booster dose and contributed solicited adverse reaction data.

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

[a] Grade 3 pain and axillary swelling/tenderness: Defined as any use of prescription pain reliever; prevents daily activity.

[b] Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.

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

[d] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.

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

[f] Grade 3 nausea/vomiting: Defined as prevents daily activity; requires outpatient intravenous hydration.

The median duration of solicited local and systemic adverse reactions was 2 days in participants who received either vaccine booster dose.

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 post-authorization use of Moderna COVID-19 Vaccine and Moderna COVID-19 Vaccine, Bivalent. 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

6.3 Required Reporting for Adverse Events and Vaccine Administration Errors

The vaccination provider enrolled in the federal COVID-19 Vaccination Program is responsible for the MANDATORY reporting of the listed events following administration of the Moderna COVID-19 Vaccine, Bivalent 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) in adults and children
- 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.

<u>Instructions for Reporting to VAERS</u>

The vaccination provider enrolled in the federal COVID-19 Vaccination Program 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)
- 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, Bivalent
- 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, Bivalent 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, Bivalent 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, Bivalent with other vaccines.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Moderna COVID-19 Vaccine, Bivalent during pregnancy. Women who are vaccinated with Moderna COVID-19 Vaccine, Bivalent during pregnancy are encouraged to enroll in the registry by calling 1-866-MODERNA (1-866-663-3762).

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 Moderna COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy. Data are not available on Moderna COVID-19 Vaccine, Bivalent administered to pregnant women.

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.

8.2 Lactation

Risk Summary

Data are not available to assess the effects of Moderna COVID-19 Vaccine, Bivalent on the breastfed infant or on milk production/excretion.

8.4 Pediatric Use

Moderna COVID-19 Vaccine, Bivalent is authorized for use in individuals 6 months through 17 years of age. This authorization is based on safety and effectiveness data with Moderna COVID-19 Vaccine in individuals 6 months of age and older, and safety and immunogenicity data with the bivalent vaccine (Original and Omicron BA.1) in adults.

Moderna COVID-19 Vaccine, Bivalent is not authorized for use in individuals younger than 6 months of age.

8.5 Geriatric Use

Clinical studies of Moderna COVID-19 Vaccine and the bivalent vaccine (Original and Omicron BA.1) included participants 65 years of age and older, and their data contribute to the overall assessment of safety and effectiveness of Moderna COVID-19 Vaccine, Bivalent. *[see Clinical Trials Experience (6.1) and Clinical Studies (14)]*. Some local and systemic adverse reactions were reported in a lower proportion of participants 65 years of age and older compared to participants 18 through 64 years of age *[see Clinical Trials Experience (6.1)]*.

In an ongoing Phase 3 clinical study (Study 1) of primary series dosing of Moderna COVID-19 Vaccine, 24.8% (n=7,520) of participants were 65 years of age and older and 4.6% (n=1,399) of participants were 75 years of age and older.

In an ongoing Phase 2/3 clinical study (Study 5) of a single booster dose of bivalent vaccine (Original and BA.1), 39.8% (n=174) were 65 years of age and older.

In a Phase 2 clinical study (Study 2) of a single booster dose of Moderna COVID-19 Vaccine, 22.2% (n=38) of participants were 65 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 17 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, Bivalent is provided as a sterile white to off-white suspension for intramuscular injection.

Each 0.2 mL dose of Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5), supplied in a multiple-dose vial with a dark pink cap and label with a yellow box, contains 5 mcg nucleoside-modified messenger RNA (mRNA) encoding the pre-fusion stabilized Spike glycoprotein (S) of the SARS-CoV-2 Wuhan-Hu-1 strain (Original) and 5 mcg mRNA encoding the pre-fusion stabilized S-protein of the SARS-CoV-2 Omicron variant lineages BA.4 and BA.5 (Omicron BA.4/BA.5). The S-proteins of the SARS-CoV-2 Omicron variant lineages BA.4 and BA.5 are identical. Each dose also contains the following ingredients: a total lipid content of 0.20 mg (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), 0.09 mg tromethamine, 0.51 mg tromethamine hydrochloride, 0.0042 mg acetic acid, 0.02 mg sodium acetate trihydrate, and 17.4 mg sucrose.

Each 0.5 mL dose of Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5), supplied in a multiple-dose vial with a dark blue cap and a label with a gray border, contains 25 mcg nucleoside-modified messenger RNA (mRNA) encoding the pre-fusion stabilized Spike glycoprotein (S) of the SARS-CoV-2 Wuhan-Hu-1 strain (Original) and 25 mcg mRNA encoding the pre-fusion stabilized S-protein of the SARS-CoV-2 Omicron variant lineages BA.4 and BA.5 (Omicron BA.4/BA.5). The S-proteins of the SARS-CoV-2 Omicron variant lineages BA.4 and BA.5 are identical. Each dose also contains the following ingredients: a total lipid content of 1.01 mg (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), 0.25 mg tromethamine, 1.2 mg tromethamine hydrochloride, 0.021 mg acetic acid, 0.10 mg sodium acetate trihydrate, and 43.5 mg sucrose. Each 0.25 mL dose of Moderna COVID-19 Vaccine, Bivalent contains half of these ingredients.

Moderna COVID-19 Vaccine, Bivalent does not contain a preservative.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

The nucleoside-modified mRNA in Moderna COVID-19 Vaccine, Bivalent 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, Bivalent is based on effectiveness of Moderna COVID-19 Vaccine and the bivalent vaccine (Original and Omicron BA.1).

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

Study 1 is an ongoing Phase 3 randomized, placebo-controlled, observer-blind clinical trial to evaluate the efficacy, safety, and immunogenicity of Moderna COVID-19 Vaccine in

participants 18 years of age and older in the United States (NCT04470427). 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 30,420 participants were randomized equally to receive 2 doses of the Moderna COVID-19 Vaccine (100 mcg mRNA per dose) or saline placebo 1 month apart. Participants will be followed for efficacy and safety until 24 months after the second dose.

The primary efficacy analysis population (referred to as the Per-Protocol Set) included 28,207 participants who received two doses (0.5 mL at 0 and 1 month) of either Moderna COVID-19 Vaccine (100 mcg mRNA; n=14,134) or placebo (n=14,073) and had a negative baseline SARS-CoV-2 status. In the Per-Protocol Set, 47.4% were female, 19.7% were Hispanic or Latino; 79.5% were White, 9.7% were African American, 4.6% were Asian, and 2.1% other races. The median age of participants was 53 years (range 18-95) and 25.3% of participants were 65 years of age and older. Of the study participants in the Per-Protocol Set, 18.5% 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. Between participants who received Moderna COVID-19 Vaccine and those who received placebo, there were no notable differences in demographics or pre-existing medical conditions.

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 / ≥100.4°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. COVID-19 cases were adjudicated by a Clinical Adjudication Committee.

The median length of follow-up for efficacy for participants in the study was 9 weeks post-Dose 2. There were 11 COVID-19 cases in the Moderna COVID-19 Vaccine group and 185 cases in the placebo group, with a vaccine efficacy of 94.1% (95% confidence interval of 89.3% to 96.8%).

Table 17: Primary Efficacy Analysis: 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			Placebo			% Vaccine Efficacy (95% CI)†
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	
14,134	11	3.328	14,073	185	56.510	94.1 (89.3, 96.8)

* COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least two systemic symptoms or one respiratory symptom. Cases starting 14 days after Dose 2.
† VE and 95% CI from the stratified Cox proportional hazard model.

The subgroup analyses of vaccine efficacy are presented in Table 18.

Table 18: Subgroup Analyses of Vaccine Efficacy: COVID-19* Cases Starting 14 Days After Dose 2 per Adjudication Committee Assessments – Per-Protocol Set

Age Subgroup (Years)	Moderna COVID-19 Vaccine			Placebo			% Vaccine Efficacy (95% CI)†
	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	
18 to <65	10,551	7	2.875	10,521	156	64.625	95.6 (90.6, 97.9)
≥65	3,583	4	4.595	3,552	29	33.728	86.4 (61.4, 95.2)

* COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least two systemic symptoms or one respiratory symptom. Cases starting 14 days after Dose 2.
† 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, no cases of severe COVID-19 were reported in the Moderna COVID-19 Vaccine group compared with 30 cases reported in the placebo group (incidence rate 9.138 per 1,000 person-years). One PCR-positive case of severe COVID-19 in a vaccine recipient was awaiting adjudication at the time of the analysis.

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

Study 3 is an ongoing Phase 2/3 randomized, placebo-controlled, observer-blind clinical trial to evaluate the safety, reactogenicity, and effectiveness of Moderna COVID-19 Vaccine in adolescents ages 12 years through 17 years in the United States (NCT04649151). Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 3,732 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. Participants will be followed for effectiveness and safety until 1 year after the last dose.

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 adolescents 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 adolescents 12 years through 17 years of age to participants 18 years through 25 years of age (Table 19).

Table 19: Summary of Geometric Mean Titer Ratio and Seroresponse Rate – Comparison of Adolescents 12 Years Through 17 Years of Age to Participants 18 Years Through 25 Years of Age – Per-Protocol Immunogenicity Subset

		Moderna COVID-19 Vaccine			
		12 Years Through 17 Years n=340	18 Years Through 25 Years n=296	12 Years Through 17 Years/ 18 Years Through 25 Years	
Assay	**Time Point**	**GMT (95% CI)***	**GMT (95% CI)***	**GMT Ratio (95% CI)[a]**	**Met Noninferiority Objective (Y/N)[b]**
SARS-CoV-2 neutralization assay – ID50 (titer)[c]	28 days after Dose 2	1401.7 (1276.3, 1539.4)	1301.3 (1177.0, 1438.8)	1.1 (0.9, 1.2)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in Seroresponse Rate % (95% CI)[e]**	
		98.8 (97.0, 99.7)	98.6 (96.6, 99.6)	0.2 (-1.8, 2.4)	

GMT = Geometric mean titers
n = Number of subjects with non-missing data at the corresponding timepoint
* 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.
[a] 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.
[b] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR 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%.
[c] 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.
[d] 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 LLOQ, or at least a 3.3-fold rise if baseline is equal to or above LLOQ. An analysis done using seroresponse definition of at least 4-fold rise from baseline, where baseline titers <LLOQ are set to LLOQ for the analysis, showed the same results. 95% CI is calculated using the Clopper-Pearson method.
[e] 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 of May 8, 2021, was performed in 3,181 participants who received two doses (at 0 and 1 month) of either Moderna COVID-19 Vaccine (n=2,139) or placebo (n=1,042) 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; 84.1% were White, 2.7% were African American, 6.3% 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. 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 for participants in the study was 53 days post-Dose 2.

The efficacy information in adolescents 12 years through 17 years of age is presented in Table 20.

Table 20: 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 N=2,139		Placebo N=1,042		% Vaccine Efficacy (95% CI)*
	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	
COVID-19 Case Definition 1[a]	0	0	4	16.525	100.0 (28.9, NE)
COVID-19 Case Definition 2[b]	1	1.939	7	28.981	93.3 (47.9, 99.9)

NE = Not estimable

***** 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.

[a] 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.

[b] 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 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 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 21).

Table 21: 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 n=320	18 Years Through 25 Years n=295	6 Years Through 11 Years/ 18 Years Through 25 Years	
Assay	**Time Point**	**GMT (95% CI)***	**GMT (95% CI)***	**GMT ratio (95% CI)[a]**	**Met Noninferiority Objective (Y/N)[b]**
SARS-CoV-2 neutralization assay – ID50 (titer)[c]	28 days after Dose 2	1610.2 (1456.6, 1780.0)	1299.9 (1171.2, 1442.7)	1.2 (1.1, 1.4)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in Seroresponse Rate % (95% CI)[e]**	
		99.1 (97.3, 99.8)	99.0 (97.1, 99.8)	0.1 (-1.9, 2.1)	

GMT = Geometric mean titer

* 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.

[a] 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.

[b] 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%.

[c] 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.

[d] 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.

[e] 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 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 22) and 2 years through 5 years of age to participants 18 years through 25 years of age (Table 23).

Table 22: 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 n=230	18 Years Through 25 Years n=291	6 Months Through 23 Months/ 18 Years Through 25 Years	
Assay	**Time Point**	**GMC (95% CI)***	**GMC (95% CI)***	**GMC Ratio (95% CI)[a]**	**Met Noninferiority Objective (Y/N)[b]**
SARS-CoV-2 neutralization assay[c]	28 days after Dose 2	1780.7 (1606.4, 1973.8)	1390.8 (1269.1, 1524.2)	1.3 (1.1, 1.5)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in Seroresponse Rate % (95% CI)[e]**	
		100 (98.4, 100)	99.3 (97.5, 99.9)	0.7 (-1.0, 2.5)	

GMC = Geometric mean concentration
n = number of participants with non-missing data at baseline and at Day 57
* 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.

[a] 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.
[b] 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%.
[c] 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.
[d] 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.
[e] Difference in seroresponse rate 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Table 23: 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 n=264	**18 Years Through 25 Years n=291**	**2 Years Through 5 Years/ 18 Years Through 25 Years**	
Assay	**Time Point**	**GMC (95% CI)***	**GMC (95% CI)***	**GMC Ratio (95% CI)[a]**	**Met Noninferiority Objective (Y/N)[b]**
SARS-CoV-2 neutralization assay[c]	28 days after Dose 2	1410.0 (1273.8, 1560.8)	1390.8 (1262.5, 1532.1)	1.0 (0.9, 1.2)	Y
		Seroresponse % (95% CI)[d]	**Seroresponse % (95% CI)[d]**	**Difference in Seroresponse Rate % (95% CI)[e]**	
		98.9 (96.7, 99.8)	99.3 (97.5, 99.9)	-0.4 (-2.7, 1.5)	

GMC = Geometric mean concentration
n = number of participants with non-missing data at baseline and at Day 57
* 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.
[a] 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.
[b] 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%.
[c] 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.

[d] 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.

[e] 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 24 and Table 25, respectively.

Table 24: 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 N=1,511		**Placebo** N=513		**% Vaccine Efficacy (95% CI)***
	Cases (n)	**Incidence Rate of COVID-19 per 1,000 Person-Years**	**Cases (n)**	**Incidence Rate of COVID-19 per 1,000 Person-Years**	
COVID-19 Cases - Definition 1[a]	37	99.981	18	146.042	31.5 (-27.7, 62.0)
COVID-19 Cases - Definition 2[b]	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.

* 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.

[a] 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.

[b] 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 25: 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 N=2,594		**Placebo** N=858		**% Vaccine Efficacy (95% CI)***
	Cases (n)	**Incidence Rate of COVID-19 per 1,000 Person-Years**	**Cases (n)**	**Incidence Rate of COVID-19 per 1,000 Person-Years**	
COVID-19 Cases - Definition 1[a]	71	103.761	43	193.528	46.4 (19.8, 63.8)
COVID-19 Cases - Definition 2[b]	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.

* 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.

[a] 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.

[b] 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 Administered as a First Booster Dose Following a Primary Series of Moderna COVID-19 Vaccine in Participants 18 Years of Age and Older

Effectiveness of a booster dose of Moderna COVID-19 Vaccine was based on 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 following the booster dose to the ID50 following the primary series.

In an open-label phase of Study 2, participants 18 years of age and older received a single booster dose (50 mcg mRNA; 0.25 mL) at least 6 months after completion of the primary series. The primary immunogenicity analysis population included 149 booster dose participants in Study 2 (including one individual who had only received a single dose of the primary series) and a random subset of 1,055 participants from Study 1 who had completed primary vaccination with Moderna COVID-19 Vaccine. Study 1 and 2 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 assessed for immunogenicity, 60.4% were female, 6.7% were Hispanic or Latino; 95.3% were White, 3.4% were Black or African American, 0.7% were Asian, and 0.7% were American Indian or Alaskan Native; 9.4% were obese (body mass index ≥30 kg/m^2). The median age of Study 2 participants was 56 years of age (range 18-82) and 24.8% of participants were 65 years of age and older. Study 2 participants included in the primary immunogenicity analysis population did not have pre-existing medical conditions that would place them at risk of severe COVID-19. Study 1 participants included in the primary immunogenicity analysis population were a stratified random sample which reflected the overall primary efficacy analysis population with regards to demographics and pre-existing medical conditions with a higher percentage of those ≥65 years of age (33.6%), with risk factors for severe COVID-19 (39.4%), and communities of color (53.5%).

Immunogenicity analyses included an assessment of ID50 geometric mean titer (GMT) ratio and difference in seroresponse rates. The analysis of the GMT ratio of ID50 following the booster dose compared to the primary series met the immunobridging criteria for a booster response. Seroresponse for a participant was defined as achieving a ≥4-fold rise in ID50 from baseline (before the booster dose in Study 2 and before the first dose of the primary series in Study 1). The lower limit of the 2-sided 95% CI for the difference in seroresponse rates between Study 1 and Study 2 was -16.7%, which did not meet the immunobridging criterion for a booster response (lower limit of 2-sided 95% CI for the percentage difference of ≥-10%). These analyses are summarized in Table 26 and Table 27.

Table 26: Neutralizing Antibody Geometric Mean Titers (ID50) 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 2 vs 28 Days After Completion of the Primary Series in Study 1, Participants ≥18 Years of Age, Per-Protocol Immunogenicity Set*

Study 2 Booster Dose N[a]=149 GMT[b] (95% CI)	Study 1 Primary Series N[a]=1,053 GMT[b] (95% CI)	GMT Ratio (Study 2/Study 1)	Met Success Criteria[c]
1802 (1548, 2099)	1027 (968, 1089)	1.8 (1.5, 2.1)	Lower limit of 95% CI ≥0.67 Criterion: Yes Point Estimate ≥1.0 Criterion: Yes

* Per-Protocol Immunogenicity Set included all subjects who had both baseline (or Study 2 Day 1 for Study 2) and

post-vaccination immunogenicity samples, did not have SARS-CoV-2 infection at baseline (or Study 2 Day 1 for Study 2), did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest (Day 29 for Study 2 and Day 57 for Study 1).

[a] Number of subjects with non-missing data at the corresponding timepoint.

[b] Given the lack of randomization in Study 2, the statistical analysis plan pre-specified an analysis of covariance model for estimating the geometric mean titer that adjusts for differences in age groups (<65 years, ≥65 years).

[c] Immunobridging is declared if the lower limit of the 2-sided 95% CI for the GMR is >0.67 and the point estimate of the GLSM ratio is ≥1.0.

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.

GLSM = Geometric least squares mean

GMR = Geometric mean ratio

Table 27: Seroresponse Rates Against a Pseudovirus Expressing the SARS-CoV-2 Spike Protein (USA_WA1/2020 isolate carrying the D614G mutation) at 28 Days Post-Booster Dose in Study 2 and 28 Days After Completion of the Primary Series in Study 1, Participants ≥18 Years of Age, Per-Protocol Immunogenicity Set*

Study 2 Booster Seroresponse[a] N[b]=149 n (%) (95% CI)[c]	Study 1 Primary Series Seroresponse[a] N[b]=1,050 n (%) (95% CI)[c]	Difference in Seroresponse Rate (Study 2-Study 1) % (95% CI)[d]	Met Success Criterion[e]
131 (87.9) (81.6, 92.7)	1033 (98.4) (97.4, 99.1)	-10.5 (-16.7, -6.1)	Lower limit of 95% CI ≥-10% Criterion: No

* Per-Protocol Immunogenicity Set included all subjects who had both baseline (or Study 2 Day 1 for Study 2) and post-vaccination immunogenicity samples, did not have SARS-CoV-2 infection at baseline (or Study 2 Day 1 for Study 2), did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest (Day 29 for Study 2 and Day 57 for Study 1).

[a] Seroresponse is defined as ≥4-fold rise of pseudovirus neutralizing antibody titers (ID50) from baseline (pre-booster dose in Study 2 and pre-Dose 1 in Study 1), where baseline titers < LLOQ are set to LLOQ for the analysis.

[b] Number of subjects with non-missing data at both baseline and the post-baseline timepoint of interest.

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

[d] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

[e] Immunobridging is declared if the lower limit of the 2-sided 95% CI for the percentage difference is >-10%.

Study 2 participants who met the ≥4-fold increase in titer post-booster dose (87.9%) had a lower baseline GMT of 109 (range of individual titers 9, 4393), whereas Study 2 participants who did not meet the ≥4-fold increase in titers post-booster had a higher baseline GMT of 492 (range of individual titers 162, 2239).

An additional descriptive analysis evaluated seroresponse rates using baseline neutralizing antibody titers prior to Dose 1 of the primary series. As shown in Table 28 below, the booster dose seroresponse rate, with seroresponse defined as at least a 4-fold rise relative to the pre-Dose 1 titer, was 100%. The difference in seroresponse rates in this post-hoc analysis was 1.6% (95% CI -0.9, 2.6).

Table 28: Analysis of Seroresponse Rates Against a Pseudovirus Expressing the SARS-CoV-2 Spike Protein (USA_WA1/2020 isolate carrying the D614G mutation) at 28 Days Post-Booster Dose in Study 2 and 28 Days After Completion of the Primary Series in Study 1, Participants ≥18 Years of Age, Per-Protocol Immunogenicity Set*

Study 2 Booster Seroresponse[a] N[b]=148 n (%) (95% CI)[d]	Study 1 Primary Series Seroresponse[a] N[c]=1,050 n (%) (95% CI)[d]	Difference in Seroresponse Rate (After Booster-After Primary Series) % (95% CI)[e]
148 (100) (97.5, 100)	1033 (98.4) (97.4, 99.1)	1.6 (-0.9, 2.6)

* Per-Protocol Immunogenicity Set included all subjects who had non-missing data at baseline (before Dose 1) and 28 days post-booster in Study 2 or 28 days post-Dose 2 in the primary series in Study 1, respectively, did not have SARS-CoV-2 infection at pre-booster in Study 2 or baseline in Study 1, did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest.

[a] Seroresponse is defined as ≥4-fold rise of pseudovirus neutralizing antibody titers (ID50) from pre-Dose 1, where baseline titers < LLOQ are set to LLOQ for the analysis.

[b] Number of subjects with non-missing data at baseline (before Dose 1) and 28 days post-booster in Study 2.

[c] Number of subjects with non-missing data at baseline (before Dose 1) and 28 days post-Dose 2 in the primary series in Study 1.

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

[e] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

14.6 Immunogenicity of Moderna COVID-19 Vaccine Booster Dose Following Moderna COVID-19 Vaccine Primary Series in Participants 12 Years Through 17 Years of Age

Effectiveness of a booster dose of Moderna COVID-19 Vaccine 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 years through 25 years of age.

In an open-label phase of Study 3, participants 12 years through 17 years of age received a single booster dose of Moderna COVID-19 Vaccine (50 mcg mRNA) at least 5 months after completion of the primary series (two doses 1 month apart). The primary immunogenicity analysis population included 257 booster dose participants in Study 3 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 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. Among participants 12 years through 17 years assessed for immunogenicity, 51.0% were male, 49.0%% were female, 12.5% were Hispanic or Latino; 87.5% were White, 1.6% were Black or African American, 3.5% were Asian, 0.0% were American Indian or Alaskan Native, 0.0% were Native Hawaiian or Pacific Islander, 1.2% were other races, and 5.8% were Multiracial.

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). These analyses are summarized in Table 29.

Table 29: 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 3 (Participants 12 Years Through 17 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 3* Booster Dose N[a]=257 GMC (95% CI)	**Study 1† Primary Series N[a]=294 GMC (95% CI)**	**GMC Ratio (Study 3/Study 1)**	**Met Success Criteria**
7172 (6610, 7781)	1400 (1273, 1541)	5.1 (4.5, 5.8)	Yes[b]
Study 3 Booster Dose Seroresponse[c] N=257 n/N1 (%) (95% CI)[d]	**Study 1 Primary Series Seroresponse[c] N=294 n/N1 (%) (95% CI)[d]**	**Difference in Seroresponse Rate (Study 3-Study 1) % (95% CI)[e]**	**Met Success Criterion**
257/257 (100) (98.6, 100)	292/294 (99.3) (97.6, 99.9)	0.7 (-0.8, 2.4)	Yes[f]

***** Per-Protocol Immunogenicity Subset – Pre-Booster SARS-CoV-2 Negative for Study 3 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).

† 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).

[a] Number of subjects with non-missing data at the corresponding timepoint.

[b] Immunobridging success is declared if the lower limit of the 2-sided 95% CI for the GMC Ratio is ≥0.667 and the point estimate of the GMC Ratio is ≥0.8.

[c] Seroresponse is defined as ≥4-fold rise of pseudovirus neutralizing antibody concentration from baseline (pre-Dose 1 of primary series in Study 3 and Study 1), where baseline concentration < LLOQ is set to LLOQ for the analysis.

N1=number of participants with non-missing data at pre-vaccination baseline and 28 days post-Booster Dose for Study 3 or 28 days post-Dose 2 for Study 1.

n=number of participants who achieved seroresponse at 28 days post-Booster Dose for Study 3 or 28 days post-Dose 2 for Study 1.

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

[e] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

[f] 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 96.5%. The difference in seroresponse rates in this post-hoc analysis was -2.8% (95% CI -5.9, -0.6).

14.7 Immunogenicity of Moderna COVID-19 Vaccine Booster Dose Following Moderna COVID-19 Vaccine 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 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 30.

Table 30: 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* Booster Dose N[a]=95 GMC (95% CI)	**Study 1† Primary Series N[a]=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[b]
Study 4 Booster Dose Seroresponse[c] N=95 n/N1 (%) (95% CI)[d]	**Study 1 Primary Series Seroresponse[c] N=294 n/N1 (%) (95% CI)[d]**	**Difference in Seroresponse Rate (Study 4-Study 1) % (95% CI)[e]**	**Met Success Criterion**
88/88 (100) (95.9, 100)	292/294 (99.3) (97.6, 99.9)	0.7 (-3.5, 2.4)	Yes[f]

* 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).

† 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).

[a] Number of subjects with non-missing data at the corresponding timepoint.

[b] Immunobridging success is declared if the lower limit of the 2-sided 95% CI for the GMC Ratio is ≥0.667.

[c] 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.

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.

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.

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

[e] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

[f] 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).

14.8 Immunogenicity of Moderna COVID-19 Vaccine Booster Dose Following Moderna COVID-19 Vaccine 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 31.

Table 31: 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* Booster Dose N[a]=56 GMC (95% CI)	**Study 1† Primary Series N[a]=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[b]
Study 4 Booster Dose Seroresponse[c] N=56 n/N1 (%) (95% CI)[d]	**Study 1 Primary Series Seroresponse[c] N=294 n/N1 (%) (95% CI)[d]**	**Difference in Seroresponse Rate (Study 4-Study 1) % (95% CI)[e]**	**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[f]

* 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).

† 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).

[a] Number of subjects with non-missing data at the corresponding timepoint.

[b] Immunobridging success is declared if the lower limit of the 2-sided 95% CI for the GMC Ratio is ≥0.667.

[c] 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.

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.

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.

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

[e] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

[f] 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).

14.9 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 is 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 32 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 33).

Table 32: 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) N=334 GMT[a] (95% CI)	Moderna COVID-19 Vaccine N=260 GMT[a] (95% CI)	GMT Ratio[a] (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[b]
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[c]

* 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] 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.

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

[c] Non-inferiority 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 33: 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) Seroresponse[a] N=334 n/N1 (%) (95% CI)[b]	Moderna COVID-19 Vaccine Seroresponse[a] N=260 n/N1 (%) (95% CI)[b]	Difference in Seroresponse Rate (Bivalent Vaccine [Original and Omicron BA.1]-Moderna COVID-19 Vaccine) % (97.5% CI)[c]
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.
N1=number of participants with non-missing data at pre-booster baseline and 28 days after second booster dose.
n=number of participants who achieved seroresponse at 28 days after booster dose.
[a] 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.
[b] 95% CI is calculated using the Clopper-Pearson method.
[c] Common risk difference and 97.5% CI is calculated using the stratified Miettinen-Nurminen method to adjust for age group (<65, ≥65 years).

14.10 Immunogenicity of a Single Dose of Moderna COVID-19 Vaccine 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 34 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.

Table 34: 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 ≥18 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, Bivalent (Original and Omicron BA.4/BA.5): multiple-dose vials with dark pink caps and labels with a yellow box.

NDC 80777-283-99	Carton of 10 multiple-dose vials
NDC 80777-283-02	Multiple-dose vial containing 2 doses of 0.2 mL

Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5): multiple-dose vials with dark blue caps and labels with a gray border.

NDC 80777-282-99	Carton of 10 multiple-dose vials
NDC 80777-282-05	Multiple-dose vial containing 2.5 mL
	Both 0.5 mL doses and 0.25 mL doses may be withdrawn from the same multiple-dose vial. If withdrawing only 0.5 mL doses, each multiple-dose vial contains 5 doses. If withdrawing only 0.25 mL doses, each multiple-dose vial contains 10 doses.

Storage and Handling

Minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

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

Storage after Thawing
- Storage at 2°C to 8°C (36°F to 46°F):
    - Vials may be stored refrigerated between 2°C to 8°C (36°F to 46°F) for up to 30 days prior to first use, provided the expiration date is not exceeded.
    - Vials with a pink cap and label with a yellow box: Discard 8 hours after the first puncture.

    - Vials with dark blue caps and labels with a gray border: Discard 12 hours after the first puncture.
    -
- Storage at 8°C to 25°C (46°F to 77°F):
    - Vials may be stored between 8°C to 25°C (46°F to 77°F) for a total of 24 hours.
    - Vials with a pink cap and label with a yellow box: Discard 8 hours after the first puncture.
    - Vials with dark blue caps and labels with a gray border: Discard 12 hours after the first puncture.
    - Total storage at 8°C to 25°C (46°F to 77°F) must not exceed 24 hours.

Do not refreeze once thawed.

Thawed vials can be handled in room light conditions.

Transportation of Thawed Vials at 2°C to 8°C (36°F to 46°F)
If transport at -50°C to -15°C (-58°F to 5°F) is not feasible, available data support transportation of one or more thawed vials for up to 12 hours at 2°C to 8°C (36°F to 46°F) when shipped using shipping containers which have been qualified to maintain 2°C to 8°C (36°F to 46°F) and under routine road and air transport conditions with shaking and vibration minimized. Once thawed and transported at 2°C to 8°C (36°F to 46°F), vials 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.

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Princeton, NJ 08540

Patent(s): www.modernatx.com/patents
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