U.S. FOOD & DRUG ADMINISTRATION

April 18, 2023

ModernaTX, Inc.
Attention: Ms. Michelle Olsen
200 Technology Square
Cambridge, MA 02139

Dear Ms. Olsen:

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

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

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

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

FDA reissued the letter of authorization on: February 25, 2021,[3] July 7, 2021,[4] August 12, 2021,[5] October 20, 2021,[6] November 19, 2021,[7] and January 7, 2022.[8] On January 31, 2022, FDA approved SPIKEVAX (COVID-19 Vaccine, mRNA)[9] and reissued the letter in its entirety for both Moderna COVID-19 Vaccine and certain uses of SPIKEVAX (COVID-19 Vaccine, mRNA).[10]

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

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

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

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

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

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

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

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

Subsequently, FDA reissued the letter of authorization on March 15, 2022,[11] March 29, 2022,[12] June 17, 2022,[13] and August 31, 2022.[14] The August 31, 2022 reissuance provided for certain emergency uses of the Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)[15] after either completion of primary vaccination with any FDA approved or authorized monovalent[16] COVID-19 vaccine or receipt of the most recent booster dose with any

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

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

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

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

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

[16] For purposes of this letter, monovalent refers to any COVID-19 Vaccine that contains or encodes the spike protein of only the Original SARS-CoV-2.

FDA authorized or approved monovalent COVID-19 vaccine. Subsequently, FDA reissued the letter of authorization on October 12, 2022,[17] and December 8, 2022.[18]

On April 18, 2022, having concluded that revising this EUA is appropriate to protect the public health or safety under section 564(g)(2) of the Act, FDA is reissuing the December 8, 2022 letter of authorization in its entirety with revisions to:

1. Revise the authorized dosing regimen and schedule of the Moderna COVID-19 Vaccine, Bivalent, as described in the Scope of Authorization (Section II);
2. No longer authorize use of the Moderna COVID-19 Vaccine and certain uses of SPIKEVAX (COVID-19 Vaccine; mRNA) in the United States;
3. Clarify the terms and conditions that relate to export of Moderna COVID-19 Vaccine from the United States; and
4. Revise Condition G to require the inclusion of distribution data for Moderna COVID-19 Vaccine and Moderna COVID-19 Vaccine, Bivalent in the monthly periodic safety reports.

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

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

FDA is revising the applicable Fact Sheets for Moderna COVID-19 Vaccine, Bivalent, to reflect these changes. In addition, the Fact Sheets for Healthcare Providers Administering Vaccine (Vaccination Providers) have been consolidated into a single Fact Sheet for Healthcare Providers Administering Vaccine for all authorized presentations of Moderna COVID-19 Vaccine, Bivalent; and the Fact Sheets for Recipient and Caregivers have been consolidated into a single Fact Sheet for Recipients and Caregivers for all authorized presentations of Moderna COVID-19 Vaccine, Bivalent.

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

For the August 12, 2021 authorization of a third primary series dose of the Moderna COVID-19 vaccine in individuals 18 years of age or older who have undergone solid organ transplantation, or individuals 18 years of age or older who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise, FDA reviewed safety and effectiveness data reported in two manuscripts on solid organ transplant recipients. The first study was a double-blind, randomized-controlled study conducted in 120 individuals who had undergone various solid organ transplant procedures (heart, kidney, kidney-pancreas, liver, lung, pancreas) a median of 3.57 years earlier (range 1.99-6.75 years). A third dose of the Moderna COVID-19 vaccine was administered to 60 individuals approximately 2 months after they had received a second dose (i.e., doses at 0, 1 and 3 months); saline placebo was given to 60 individuals or comparison. The primary outcome was anti-RBD antibody at 4 months greater than 100 U/mL. This titer was selected based on NHP challenge studies as well as a large clinical cohort study to indicate this

antibody titer was possibly protective. Secondary outcome was based on a virus neutralization assay polyfunctional T cell responses. Baseline characteristics were comparable between the two study arms as were pre-intervention anti-RBD titer and neutralizing antibodies. Levels of SARS-CoV-2 antibodies indicative of a significant response occurred four weeks after the third dose in 33/60 (55.0%) of the Moderna COVID-19 vaccinated group and 10/57 (17.5%) of the placebo individuals. In the 60 individuals who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 adverse events were reported. A supportive secondary study describes a single arm study conducted in 101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) a median of 97±8 months earlier. A third dose of a similar messenger RNA COVID-19 vaccine, Pfizer-BioNTech COVID-19, was administered to 99 of these individuals approximately 2 months after they had received a second dose. Levels of SARS-CoV-2 antibodies meeting the pre-identified criteria for success occurred four weeks after the third dose in 26/59 (44.0%) of those who were initially considered to be seronegative and received a third dose of the Pfizer-BioNTech COVID-19 vaccine; 67/99 (68%) of the entire group receiving a third vaccination had an increase in antibody titers that the investigators considered significant. In those who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported. Despite the moderate enhancement in antibody titers, the totality of data (including the supportive paper by Kamar et al. and demonstrated efficacy of the product in the elderly and persons with co-morbidities) supports the conclusion that a third dose of the Moderna COVID-19 vaccine may be effective in this population, and that the known and potential benefit of a third dose of Moderna COVID-19 vaccine outweigh the known and potential risks of the vaccine for immunocompromised individuals at least 18 years of age who have received two doses of the Moderna COVID-19 vaccine and who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

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

for a booster response were met for a comparison of the ID50 geometric mean titers and that the immunobridging criterion for a booster response was not met for a comparison of ID50 seroresponse rates. Based on the totality of the scientific evidence available, including data from the above-referenced clinical trials, FDA concluded that a booster dose of the Moderna COVID-19 Vaccine may be effective, and that the known and potential benefits of a single booster dose at least 6 months after completing the primary series outweigh the known and potential risks for individuals 65 years of age and older, individuals 18 through 64 years of age at high risk of severe COVID-19, and individuals 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2.

For the October 20, 2021 authorization of a single booster dose of the Moderna COVID-19 Vaccine as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine, FDA reviewed data from an ongoing Phase1/2 clinical trial in participants 19-85 years of age. In this study, adults who had completed primary vaccination with 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 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 (0.5 mL), 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 (0.5 mL) 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 (0.25 mL). Neutralizing antibody titers, as measured by a pseudovirus neutralization assay using a lentivirus expressing the SARS-CoV-2 Spike protein with D614G mutation, were assessed on Day 1 prior to administration of the booster dose and on Day 15 after the booster dose. A booster response to the Moderna COVID-19 Vaccine 100 mcg (0.5 mL) was demonstrated regardless of primary vaccination. FDA also considered immunogenicity data from manufacturer-conducted clinical trials that evaluated both a 0.25 mL dose and a 0.5 mL dose of the Moderna COVID-19 Vaccine for the first dose of the primary series and a 0.25 mL dose for a homologous booster dose. Based on the totality of the scientific evidence available, including data from the above-referenced clinical trial, FDA concluded that a heterologous booster dose (0.25 mL) of the Moderna COVID-19 Vaccine may be effective, and that the known and potential benefits of a heterologous booster dose of the Moderna COVID-19 Vaccine following completion of primary vaccination with another authorized or approved COVID-19 vaccine outweigh the known and potential risks.

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

booster dose to include all individuals 18 years of age and older who completed the primary series at least 6 months previously. Data previously reviewed to support the October 20, 2021, authorization of a heterologous booster dose, together with data and information to support authorization of the EUA amendment to expand the eligible population for a homologous booster dose of the Pfizer-BioNTech Vaccine, support a revision to the Moderna COVID-19 Vaccine EUA such that the eligible population for a heterologous booster dose of the Moderna COVID-19 Vaccine is all adults 18 years of age and older who completed primary vaccination with another authorized or approved COVID-19 vaccine. Based on the totality of the scientific evidence available, FDA concluded that a homologous or heterologous booster dose of the Moderna COVID-19 Vaccine may be effective, and that the known and potential benefits of the booster dose of the Moderna COVID-19 Vaccine following completion of primary vaccination with Moderna COVID-19 Vaccine or another authorized or approved COVID-19 vaccine outweigh the known and potential risks in individuals 18 years of age and older.

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

For the March 29, 2022 authorization of a second booster dose of the Moderna COVID-19 Vaccine for administration to individuals 50 years of age and older and to individuals 18 years of age or older with certain kinds of immunocompromise at least 4 months after receipt of a first booster dose of any FDA authorized or approved COVID-19 vaccine, the sponsor provided a publication of an ongoing, open label, non-randomized study conducted in healthcare workers at a single site in Israel. (*Gili Regev-Yochay, Tal Gonen, Mayan Gilboa, et al. 2022 DOI: 10.1056/NEJMc2202542*). In this study, 120 individuals 18 years of age and older who had received primary vaccination and a first booster dose with Pfizer-BioNTech COVID-19 Vaccine were administered a second booster dose of Moderna COVID-19 Vaccine at least four months after the first booster dose. Among these individuals, approximately 7- to 16-fold increases in geometric mean neutralizing antibody titers against wild-type virus and Delta and Omicron variants, were reported at two weeks after the second booster as compared to 5 months after the first booster dose. No new safety concerns were reported during up to three weeks of follow up

after the second booster dose. Based on the totality of the scientific evidence available, FDA concluded that a second booster dose of the Moderna COVID-19 Vaccine may be effective and that the known and potential benefits of a second booster dose of the Moderna COVID-19 Vaccine following receipt of a first booster dose of any FDA authorized or approved COVID-19 vaccine outweigh the known and potential risks in the authorized populations when given at least 4 months following the first booster dose.

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

For the June 17, 2022 authorization of the Moderna COVID-19 Vaccine for individuals 6 months through 17 years of age, and the two new presentations of the Moderna COVID-19 Vaccine, FDA reviewed safety and effectiveness data from two ongoing studies, Study 3 and Study 4. Study 3 is an ongoing Phase 2/3 trial that has enrolled 3,726 participants 12 through 17 years of age, of whom 2,486 participants received at least one dose of Moderna COVID-19 Vaccine (containing 100 mcg mRNA per dose) and 1,240 participants received saline placebo. Participants with a known history of SARS-CoV-2 infection were excluded from the study. FDA's review of the available safety data among 2,486 participants who received Moderna COVID-19 Vaccine and had a median follow-up duration of 53 days after the second dose for blinded, placebo-controlled follow-up and 312 days after the second dose including unblinded follow-up, did not identify specific safety concerns that would preclude issuance of an EUA. Effectiveness is based on a comparison of immune responses in this age group to adults 18 through 25 years of age. SARS-CoV-2 50% neutralizing antibody titers and seroresponse rates 28 days after the second dose were compared between a subset of participants 12 through 17 years of age from Study 3 and a subset of participants 18 through 25 years of age who received Moderna COVID-19 Vaccine (containing 100 mcg mRNA per dose) in the above-referenced Study 1. Participants included in these analyses had no immunologic or virologic evidence of prior SARS-CoV-2 at baseline. FDA's analyses confirm that immunobridging criteria were met for both geometric mean antibody titers and seroresponse rates. FDA's analysis of available descriptive efficacy data from 3,181 participants 12 through 17 years of age who had a negative baseline SARS-CoV-2 status confirm that the vaccine was 93.3% effective (95% confidence interval 47.9, 99.9) in preventing COVID-19 (defined as at least one symptom of COVID-19 and a positive SARS-CoV-2 test). The median length of follow up for efficacy for participants in the

study was 53 days post Dose 2. Study 4 is an ongoing Phase 2/3 trial that has enrolled 4,002 participants 6 years through 11 years of age, of whom 3,007 participants received at least one dose of Moderna COVID-19 Vaccine (50 mcg mRNA per dose) and 995 participants received saline placebo. Participants with a known history of SARS-CoV-2 infection within 2 weeks of study vaccination were excluded from the study. FDA's review of the available safety data among 3,007 participants who received Moderna COVID-19 Vaccine and had a median follow-up duration of 51 days after the second dose for blinded, placebo-controlled follow-up and 158 days after the second dose including unblinded follow-up, did not identify specific safety concerns that would preclude issuance of an EUA. Effectiveness in individuals 6 years through 11 years of age is based on a comparison of immune responses in this age group to adults 18 through 25 years of age. SARS-CoV-2 50% neutralizing antibody titers and seroresponse rates 28 days after the second dose were compared between a subset of participants 6 years through 11 years of age in this study to a subset of individuals 18 through 25 years of age who received Moderna COVID-19 Vaccine (containing 100 mcg mRNA) in Study 1. Participants included in these analyses had no immunologic or virologic evidence of prior SARS-CoV-2 at baseline. FDA's analyses confirm that immunobridging criteria were met for both geometric mean antibody titers and seroresponse rates. Safety and effectiveness of the Moderna COVID-19 Vaccine for individuals 6 months through 5 years of age were also evaluated in Study 4. In Study 4, 6,388 participants 6 months through 5 years of age were enrolled, of whom 4,792 received at least one dose of Moderna COVID-19 Vaccine (25 mcg mRNA per dose) and 1,596 received saline placebo. Among these participants, 4,038 participants (3,031 who received Moderna COVID-19 Vaccine and 1,007 who received placebo) were 2 through 5 years of age and 2,350 participants (1,761 who received Moderna COVID-19 Vaccine and 589 who received placebo) were 6 through 23 months of age. The median duration of blinded follow-up for safety was 71 days after Dose 2 for participants 2 through 5 years and 68 days after Dose 2 for participants 6 through 23 months of age. FDA's review of the available safety data among 4,038 participants 2 through 5 years of age and 2,350 participants 6 through 23 months of age did not identify specific safety concerns that would preclude issuance of an EUA. Effectiveness in individuals 6 months through 5 years of age is based on a comparison of immune responses in this age group to adults 18 through 25 years of age. SARS-CoV-2 neutralizing antibody concentrations and seroresponse rates 28 days after the second dose were compared between a subset of participants 2 through 5 years of age in Study 4 and a subset of participants 18 through 25 years of age in Study 1, and between a subset of participants 6 through 23 months in Study 4 and a subset of participants 18 through 25 years of age in Study 1. Participants included in these analyses had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. FDA's analyses confirm that for both age groups, 2 through 5 years and 6 through 23 months, immunobridging criteria were met for both geometric mean antibody concentrations and seroresponse rates. FDA's analysis of available descriptive efficacy data from 5,476 participants 6 months through 5 years of age show that the vaccine was 36.8% effective (95% confidence interval 12.5, 54.0) in preventing COVID-19 (defined as at least one symptom of COVID-19 and a positive SARS-CoV-2 test) in individuals 2 through 5 years of age and 50.6% effective (95% confidence interval 21.4, 68.6) in individuals 6 through 23 months of age. The median length of follow-up for efficacy post-Dose 2 was 71 days for participants 2 through 5 years of age and 68 days for participants 6 through 23 months of age. Based on these data, FDA concluded that it is reasonable to believe that Moderna COVID-19 Vaccine may be effective in individuals 6 months

through 17 years of age. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Moderna COVID-19 Vaccine outweigh the known and potential risks of the vaccine for the prevention of COVID-19 in individuals 6 months through 17 years of age. On June 14, 2022, the Vaccines and Related Biological Products Advisory Committee voted in agreement with this conclusion for individuals 6 through 17 years. On June 15, 2022, the Vaccines and Related Biological Products Advisory Committee voted in agreement with this conclusion for individuals 6 months through 5 years of age.

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

The August 31, 2022 authorization of a booster dose of the Moderna COVID-19 Vaccine, Bivalent, in individuals 18 years of age and older is based on: 1) safety and effectiveness data from clinical trials which evaluated primary and booster vaccination with Moderna COVID-19 Vaccine; 2) postmarketing safety data with Moderna COVID-19 Vaccine; and 3) safety and immunogenicity data from a clinical trial (Study 5) which evaluated a booster dose of Moderna's bivalent COVID-19 vaccine (Original and Omicron BA.1), not authorized or approved in the U.S., hereafter referred to as bivalent vaccine (Original and Omicron BA.1). FDA considered safety and effectiveness data previously reviewed by FDA in support of the December 18, 2020 and June 17, 2022 authorizations of primary vaccinations and the October 20, 2021, November 19, 2021, January 7, 2022, and March 29, 2022 authorizations of booster vaccinations in individuals 18 years and older with Moderna COVID-19 Vaccine, as well as postmarketing safety data. Study 5 is a Phase 2/3 open-label study that evaluated the immunogenicity, safety, and reactogenicity of a booster dose of the bivalent vaccine (Original and Omicron BA.1) compared to a booster dose of Moderna COVID-19 Vaccine 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 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. 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. FDA's review of the safety data accrued with the bivalent vaccine (Original and Omicron BA.1) together with the previously submitted safety data from clinical trials and postmarketing safety data with Moderna COVID-19 Vaccine did not identify specific safety concerns that would preclude issuance of an EUA. In Study 5, primary immunogenicity analyses evaluated 50% inhibitory dose (ID50) neutralizing antibody geometric mean titers (GMTs) and seroresponse rates (the proportion achieving a ≥4-fold rise in ID50 from pre-dose 1 of the primary series) 28 days following a second booster dose with bivalent vaccine (Original and Omicron BA.1) relative to those following a second booster dose with Moderna COVID-19 Vaccine. Primary analyses of GMTs met predefined success criteria for superiority against Omicron BA.1 and noninferiority against the Original strain. The primary analysis of seroresponse against Omicron BA.1 met the criterion for noninferiority. Post-hoc analyses evaluated seroresponse rates (the proportion achieving a ≥4-fold rise in ID50 from pre-second booster) against both the Original strain and Omicron BA.1. The lower limit of the 2-sided 97.5% CI for the percentage difference in seroresponse rate (bivalent vaccine [Original and Omicron BA.1] minus Moderna COVID-19 Vaccine) was 12.9 against Omicron BA.1 and 2.1 against the Original strain. Based on the totality of the scientific evidence available, including these data and previously submitted data on the effectiveness of primary and booster vaccination with Moderna COVID-19 Vaccine in individuals 18 years of age and older, FDA concluded that it is reasonable to believe that Moderna COVID-19 Vaccine, Bivalent may be effective as a booster dose in individuals 18 years of age and older when administered at least 2 months after completion of primary vaccination or receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Moderna COVID-19 Vaccine, Bivalent outweigh the known and potential risks of the vaccine for the prevention of COVID-19 in individuals 18 years of age and older when administered at least 2 months after completion of primary vaccination or receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine. In addition, authorization of Moderna COVID-19 Vaccine, Bivalent was considered for the express purpose of improving protection conferred by COVID-19 vaccine booster doses against the currently circulating Omicron variant of SARS-CoV-2, resulting in a more favorable anticipated benefit/risk balance compared to Moderna COVID-19 Vaccine. Consequently, revising this EUA to no longer provide for the use of the Moderna COVID-19 Vaccine as a booster dose was appropriate for the protection of public health.

The October 12, 2022 authorization of a booster dose of Moderna COVID-19 Vaccine, Bivalent in individuals 6 years through 17 years of age is based on the data that FDA relied on for the August 31, 2022 authorization of the Moderna COVID-19 Vaccine, Bivalent in individuals 18 years of age and older. In addition, FDA reviewed data regarding the use of the monovalent Moderna COVID-19 Vaccine as a booster dose in individuals 6 years through 11 years of age and 12 through 17 years of age. Safety and effectiveness data for a booster dose of Moderna COVID-19 Vaccine in individuals 12 through 17 years of age were collected in Study 3, an ongoing Phase 2/3 clinical trial described above. The open-label booster portion of the study involved 1,364 participants 12 years through 17 years of age who received a booster dose of Moderna COVID-19 Vaccine at least 5 months after the second dose of the primary series. As of

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

that the known and potential benefits of Moderna COVID-19 Vaccine, Bivalent outweigh the known and potential risks of the vaccine for the prevention of COVID-19 in individuals 6 years through 17 years of age when administered at least 2 months after completion of primary vaccination or receipt of the most recent booster dose with any FDA authorized or approved monovalent COVID-19 vaccine.[19]

The December 8, 2022 authorization of a booster dose of Moderna COVID-19 Vaccine, Bivalent in individuals 6 months through 5 years of age is based on data that FDA relied on for the August 31, 2022 authorization of the Moderna COVID-19 Vaccine, Bivalent in individuals 18 years of age and older. In addition, FDA reviewed postmarketing safety data with Moderna COVID-19 Vaccine and Moderna COVID-19 Vaccine, Bivalent, and safety and immunogenicity data regarding the use of the monovalent Moderna COVID-19 Vaccine as a booster dose in individuals 17 months through 5 years of age collected in Study 4. Study 4 is an ongoing Phase 2/3 Study with multiple parts. The open-label booster portion of the study involved 145 participants 17 months through 5 years of age who received a booster dose of Moderna COVID-19 Vaccine (10 mcg mRNA) at least 6 months after the completion of the Moderna COVID-19 Vaccine two-dose primary series. As of the data cutoff date of August 18, 2022, the median duration of follow-up for safety after the booster dose was 99 days. The primary immunogenicity analysis population included 56 booster dose participants in Study 4 and a random subset of 295 participants 18 through 25 years from Study 1 who had completed primary vaccination with two doses of Moderna COVID-19 Vaccine (100 mcg mRNA per dose) 1 month apart. Study 1 and 4 participants included in the analysis population had no serologic or virologic evidence of SARS-CoV-2 infection prior to the first primary series dose and prior to the booster dose, respectively. The primary immunogenicity analyses of the GMC ratio and difference in seroresponse rates following the booster dose in Study 4 compared to following the primary series in Study 1 met the pre-defined immunobridging success criteria. Seroresponse for a participant was defined as achieving a ≥4-fold rise of neutralizing antibody concentration from baseline (before the first dose of the primary series in Study 4 and Study 1). In a descriptive analysis, the booster dose seroresponse rate among participants 17 months through 5 years of age with seroresponse defined as at least a 4-fold rise relative to the pre-booster concentration, was 94.6%. The difference in seroresponse rates (Study 4 participants minus Study 1 participants) in this post-hoc analysis was -4.7% (95% CI -14.0, -0.9). Based on the totality of the scientific evidence available, FDA concluded that it is reasonable to believe that Moderna COVID-19 Vaccine, Bivalent may be effective as a booster dose in individuals 6 months through 5 years of age when administered at least 2 months after completion of primary vaccination with Moderna COVID-19 Vaccine. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Moderna COVID-19 Vaccine, Bivalent outweigh the known and potential risks of the vaccine for the prevention of COVID-19 in individuals 6 months through 5 years of age when administered at least 2 months after completion of primary vaccination with Moderna COVID-19 Vaccine.

For the April 18, 2023 authorization, the effectiveness of Moderna COVID-19 Vaccine, Bivalent for individuals 6 months of age and older is based on previously reviewed data on 1) effectiveness of Moderna COVID-19 Vaccine and 2) immunogenicity of the bivalent vaccine (Original and Omicron BA.1). The effectiveness of a single dose of Moderna COVID-19 Vaccine, Bivalent for most individuals 6 years of age and older is based on seroprevalence surveys that estimate that almost all of the U.S. population 5 years of age and older now have antibodies (from vaccination and/or infection) against SARS-CoV-2 (*Centers for Disease Control and Prevention. COVID Data Tracker. Atlanta, GA: US Department of Health and Human Services, CDC; 2023, March 31. https://covid.cdc.gov/covid-data-tracker*) and a comparison of neutralizing antibody titers against a pseudovirus expressing the original SARS-CoV-2 Spike protein (D614G) at baseline (pre-Dose 1), at 28 days after Dose 1 for participants with evidence of prior SARS-CoV-2 infection, and at 28 days after Dose 2 for participants without evidence of prior SARS-CoV-2 infection. These data are from Study 4 and Study 1 evaluating a primary series of Moderna COVID-19 Vaccine for the following age groups: 6 years through 11 years of age and 18 years of age and older, respectively. In both age groups, neutralizing antibody titers at 28 days post-Dose 1 in participants with evidence of prior infection were not statistically different from those of participants without evidence of prior infection at 28 days post-Dose 2. The safety of Moderna COVID-19 Vaccine, Bivalent in individuals 6 months of age and older is based on previously reviewed safety data from clinical studies which evaluated primary and booster vaccination with Moderna COVID-19 Vaccine, and 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. FDA's review of the available safety data in individuals 6 months of age and older did not identify specific safety concerns that would preclude issuance of an EUA. Based on the totality of the scientific evidence available, FDA concluded that it is reasonable to believe that Moderna COVID-19 Vaccine, Bivalent may be effective in individuals 6 months of age and older for the prevention of COVID-19 when administered in accordance with the revised dosing regimen and schedule. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Moderna COVID-19 Vaccine, Bivalent when administered in accordance with the revised dosing regimen and schedule outweigh the known and potential risks of the vaccine for the prevention of COVID-19 in individuals 6 months of age and older. The revised dosing regimen and schedule are set forth in the Scope of Authorization (Section II). In addition, simplification of the vaccine composition (i.e., single vaccine composition for all doses) and schedule was considered for the express purpose of reducing complexity, decreasing vaccine administration errors due to the complexity of the number of different vial presentations, and potentially increasing vaccine uptake by allowing clearer communication. Revising the EUA to provide for a simplified vaccine composition and schedule in the United States, by no longer providing for the use of the monovalent Moderna COVID-19 Vaccine in the United States, is appropriate for the protection of the public health.

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

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of Moderna COVID-19 Vaccine, Bivalent[20] for the prevention of COVID-19 when administered as described in the Scope of Authorization (Section II) meets the criteria for issuance of an authorization under Section 564(c) of the Act, because:

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

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

C. There is no adequate, approved, and available alternative[21] to the emergency use of Moderna COVID-19 Vaccine, Bivalent to prevent COVID-19.[22]

II. Scope of Authorization

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

- ModernaTX, Inc. will supply Moderna COVID-19 Vaccine, Bivalent and Moderna COVID-19 Vaccine either directly or through authorized distributor(s)[23] to

[20] In this section (Section I), references to Moderna COVID-19 Vaccine, Bivalent also apply to Moderna COVID-19 Vaccine.

[21] Although SPIKEVAX (COVID-19 Vaccine, mRNA) and Comirnaty (COVID-19 Vaccine, mRNA) are approved to prevent COVID-19 in certain individuals who fall within the scope of the Moderna COVID-19 Vaccine, Bivalent authorization, there is not sufficient approved vaccine available for distribution to this population in its entirety at the time of reissuance of this EUA. Additionally, there are no COVID-19 vaccines that are approved to provide additional doses to certain immunocompromised populations as described in this EUA or COVID-19 vaccination in individuals younger than 12 years of age. In addition, there are no bivalent vaccines that contain or encode the spike protein of the Omicron variant of SARS-CoV-2 that are approved to prevent COVID-19.

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

[23] "Authorized Distributor(s)" are identified by ModernaTX, Inc. or, if applicable, by a U.S. government entity, such as the Centers for Disease Control and Prevention (CDC) and/or other designee, as an entity or entities allowed to distribute authorized Moderna COVID-19 Vaccine, Bivalent or Moderna COVID-19 Vaccine.

emergency response stakeholders[24] as directed by the U.S. government, including the Centers for Disease Control and Prevention (CDC) and/or other designee, for use consistent with the terms and conditions of this EUA;

- Moderna COVID-19 Vaccine, Bivalent and Moderna COVID-19 Vaccine may be administered by a vaccination provider[25] without an individual prescription for each vaccine recipient; and
- The presentations of the Moderna COVID-19 Vaccine, Bivalent and Moderna COVID-19 Vaccine covered by this authorization, as described in more detail under *Product Description*, will be administered by vaccination providers in accordance with the uses described in the Scope of Authorization (Section II).

[24] For purposes of this letter, "emergency response stakeholder" refers to a public health agency and its delegates that have legal responsibility and authority for responding to an incident, based on political or geographical boundary lines (e.g., city, county, tribal, territorial, State, or Federal), or functional (e.g., law enforcement or public health range) or sphere of authority to administer, deliver, or distribute vaccine in an emergency situation. In some cases (e.g., depending on a state or local jurisdiction's COVID-19 vaccination response organization and plans), there might be overlapping roles and responsibilities among "emergency response stakeholders" and "vaccination providers" (e.g., if a local health department is administering COVID-19 vaccines; if a pharmacy is acting in an official capacity under the authority of the state health department to administer COVID-19 vaccines). In such cases, it is expected that the conditions of authorization that apply to emergency response stakeholders and vaccination providers will all be met.

[25] For purposes of this letter, "vaccination provider" refers to the facility, organization, or healthcare provider licensed or otherwise authorized by the emergency response stakeholder (e.g., non-physician healthcare professionals, such as nurses and pharmacists pursuant to state law under a standing order issued by the state health officer) to administer or provide vaccination services in accordance with the applicable emergency response stakeholder's official COVID-19 vaccination and emergency response plan(s) and who is enrolled in the CDC COVID-19 Vaccination Program. If the vaccine is exported from the United States, a "vaccination provider" is a provider that is authorized to administer this vaccine in accordance with the laws of the country in which it is administered. For purposes of this letter, "healthcare provider" also refers to a person authorized by the U.S. Department of Health and Human Services (e.g., under the PREP Act Declaration for Medical Countermeasures against COVID-19) to administer FDA-authorized COVID-19 vaccine (e.g., qualified pharmacy technicians and State-authorized pharmacy interns acting under the supervision of a qualified pharmacist). See, e.g., HHS. *Fourth Amendment to the Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19 and Republication of the Declaration*. 85 FR 79190 (December 9, 2020).

Table 1. Authorized Uses of Moderna COVID-19 Vaccine, Bivalent[¥] for use in Individuals 6 Months of Age and Older Not Previously Vaccinated with a 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

[¥] The labels for all Moderna COVID-19 Vaccine, Bivalent vials state "BOOSTER DOSES ONLY." Doses from the vials are authorized as described in this table.

Table 2. Authorized Uses of the Moderna COVID-19 Vaccine, Bivalent[¥] for Use in Individuals 6 Months Through 5 Years of Age Previously Vaccinated with Moderna COVID-19 Vaccine*

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[Δ]	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

[*] The monovalent Moderna COVID-19 Vaccine is no longer authorized for use in the United States.
[¥] The labels for all Moderna COVID-19 Vaccine, Bivalent vials state "BOOSTER DOSES ONLY." Doses from the vials are authorized as described in this table.
[Δ] For individuals with certain kinds of immunocompromise. See text below table 3 for dosing regimen, dose and schedule

Table 3. Authorized Uses of the Moderna COVID-19 Vaccine, Bivalent¥ in Individuals 6 Years of Age and Older Previously Vaccinated with 1 or More Doses of Any Monovalent COVID-19 Vaccine^

Age	Moderna COVID-19 Vaccine, Bivalent Vial Cap and Label Color	Dosing Regimen, Dose and Schedule
6-11 y	Dark Blue Cap and a Label with Gray Border	Single dose, 0.25 mL ≥ 2 months after monovalent COVID-19 vaccine
12-64 y	Dark Blue Cap and a Label with Gray Border	Single dose, 0.5 mL ≥ 2 months after monovalent COVID-19 vaccine
≥65 y	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

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

¥ The labels for all Moderna COVID-19 Vaccine, Bivalent vials state "BOOSTER DOSES ONLY." Doses from the vials are authorized as described in this table.

For individuals with certain kinds of immunocompromise[26] 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[27] 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 years of age and older, a single additional age-appropriate dose[28] of Moderna COVID-19 Vaccine, Bivalent may be

[26] 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.

[27] 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.

[28] For individuals 6 through 11 years of age, the authorized age-appropriate dose is a 0.25 mL dose from the presentation with a dark blue cap and a label with a gray border. For individuals 12 years of age and older, the authorized age-appropriate dose is a 0.5 mL dose from the presentation with a dark blue cap and a label with a gray border.

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.

Moderna COVID-19 Vaccine

The Moderna COVID-19 Vaccine is no longer authorized for use in the United States. However, the authorized presentations of the Moderna COVID-19 Vaccine described in Section II of the December 8, 2022 reissuance of this Letter remain authorized when exported from the United States in accordance with Section III.AA. Under Section III.AA, the Fact Sheets for Moderna COVID-19 Vaccine that were authorized as of December 8, 2022 and that describe the scope of FDA's December 8, 2022 authorization must, upon request, be made available to the regulatory authorities of the country in which the vaccine will be used.

Product Description

The Moderna COVID-19 Vaccine, Bivalent is provided in multiple dose vials:

Multiple dose vials with dark pink caps and labels with a yellow box

Each 0.2 mL dose of Moderna COVID-19 Vaccine, Bivalent, supplied in a multiple-dose vial with a dark pink cap and a label with a yellow box, contains 5 mcg 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 in Sterile Water for Injection. Moderna COVID-19 Vaccine, Bivalent does not contain a preservative.

Multiple dose vials with dark blue caps and labels with gray borders

Each 0.5 mL dose of Moderna COVID-19 Vaccine, Bivalent supplied in a multiple-dose vial with a dark blue cap and a label with a gray border contains 25 mcg 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 in Sterile Water for Injection. The Moderna COVID-19 Vaccine, Bivalent does not contain a preservative. Each 0.25 mL dose of Moderna COVID-19 Vaccine, Bivalent contains half of these ingredients.

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

For Moderna COVID-19 Vaccine, Section III.AA refers to the Fact Sheets for the Moderna COVID-19 Vaccine that were authorized under the December 8, 2022 reissuance of this Letter. Those Fact Sheets describe different presentations of the vaccine that were authorized for use in the United States as of that date and that remain authorized for export in accordance with Section III.

The Moderna COVID-19 Vaccine, Bivalent and Moderna COVID-19 Vaccine vial labels and carton labels are clearly marked for "Emergency Use Authorization." The Moderna COVID-19 Vaccine, Bivalent and Moderna COVID-19 Vaccine are authorized to be distributed, stored, further redistributed, and administered by emergency response stakeholders when packaged in the authorized manufacturer packaging (i.e., vials and cartons), despite the fact that the vial and carton labels may not contain information that otherwise would be required under the FD&C Act.

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

Fact Sheet for Healthcare Providers Administering Vaccine: Emergency Use Authorization of the Moderna COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

Fact Sheet for Recipients and Caregivers About the Moderna COVID-19 Vaccine, Bivalent Which Has Emergency Use Authorization (EUA) to Prevent Coronavirus Disease 2019 (COVID-19)

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

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that Moderna COVID-19 Vaccine, Bivalent and Moderna COVID-19 Vaccine may be effective in preventing COVID-19 when used

in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act.

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

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

III. Conditions of Authorization

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

ModernaTX, Inc. and Authorized Distributor(s)

A. ModernaTX, Inc. and authorized distributor(s) will ensure that the authorized Moderna COVID-19 Vaccine, Bivalent and Moderna COVID-19 Vaccine are distributed, as directed by the U.S. government, including CDC and/or other designee. For Moderna COVID-19 Vaccine, Bivalent, the authorized labeling (i.e., Fact Sheets) will be made available to vaccination providers, recipients, and caregivers consistent with the terms of this letter.

B. ModernaTX, Inc. and authorized distributor(s) will ensure that appropriate storage and cold chain is maintained until delivered to emergency response stakeholders' receipt sites.

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

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

E. ModernaTX, Inc. may request changes to this authorization, including to the authorized Fact Sheets. Any request for changes to this EUA must be submitted to Office of Vaccines Research and Review (OVRR)/Center for Biologics Evaluation and Research (CBER). Such changes require appropriate authorization prior to implementation.[29]

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

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

G. ModernaTX, Inc. must submit to Investigational New Drug application (IND) number 19745 periodic safety reports monthly, in accordance with a due date agreed upon with the Office of Biostatistics and Pharmacovigilance (OBPV)/CBER beginning after the first full calendar month after authorization. Each periodic safety report is required to contain descriptive information which includes:
   - A narrative summary and analysis of adverse events submitted during the reporting interval, including interval and cumulative counts by age groups,

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

special populations (e.g., pregnant women), and adverse events of special interest;
- A narrative summary and analysis of vaccine administration errors, whether or not associated with an adverse event, that were identified since the last reporting interval;
- Newly identified safety concerns in the interval;
- Actions taken since the last report because of adverse experiences (for example, changes made to Healthcare Providers Administering Vaccine (Vaccination Providers) Fact Sheet, changes made to studies or studies initiated); and
- Cumulative doses distributed, and doses distributed during the monthly reporting interval, for Moderna COVID-19 Vaccine and Moderna COVID-19 Vaccine, Bivalent.

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

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

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

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

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

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

N. ModernaTX, Inc. will conduct post-authorization observational studies to evaluate the association between Moderna COVID-19 Vaccine and Moderna COVID-19 Vaccine, Bivalent, and a pre-specified list of adverse events of special interest, including myocarditis and pericarditis, along with deaths and hospitalizations, and

severe COVID-19. The study population should include individuals administered the Moderna COVID-19 Vaccine (previously, but no longer authorized for use in the U.S.) as a primary series (6 months of age and older) or booster dose (18 years of age and older); individuals administered a dose of the Moderna COVID-19 Vaccine, Bivalent (6 months of age and older) under this EUA in the general U.S. population, and populations of interest such as healthcare workers, pregnant women, immunocompromised individuals, subpopulations with specific comorbidities. The studies should be conducted in large scale databases with an active comparator. ModernaTX, Inc. will provide protocols and status update reports to the IND 19745 with agreed-upon study designs and milestone dates.

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

Emergency Response Stakeholders

P. Emergency response stakeholders will identify vaccination sites to receive authorized Moderna COVID-19 Vaccine, Bivalent and ensure its distribution and administration, consistent with the terms of this letter and CDC's COVID-19 Vaccination Program.

Q. Emergency response stakeholders will ensure that vaccination providers within their jurisdictions are aware of this letter of authorization, and the terms herein and any subsequent amendments that might be made to the letter of authorization, instruct them about the means through which they are to obtain and administer the vaccine under the EUA, and ensure that the authorized labeling [i.e., Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) and Vaccine Information Fact Sheet for Recipients and Caregivers] is made available to vaccination providers through appropriate means (e.g., e-mail, website).

R. Emergency response stakeholders receiving authorized Moderna COVID-19 Vaccine, Bivalent will ensure that appropriate storage and cold chain is maintained.

Vaccination Providers

S. Vaccination providers will administer the vaccines in accordance with the authorization and will participate and comply with the terms and training required by CDC's COVID-19 Vaccination Program.

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

U. Vaccination providers administering the vaccines must report the following information associated with the administration of the vaccines of which they become aware to VAERS in accordance with the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers):
- 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 in children and adults
- Cases of COVID-19 that result in hospitalization or death

Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html. The VAERS reports should include the words "Moderna COVID-19 Vaccine EUA" or "Moderna COVID-19 Vaccine, Bivalent EUA," as appropriate, in the description section of the report. More information is available at vaers.hhs.gov or by calling 1-800-822-7967. To the extent feasible, report to ModernaTX, Inc., by contacting 1-866-663-3762, by providing a copy of the VAERS form to ModernaTX, Inc., Fax: 1-866-599-1342 or by email; ModernaPV@modernatx.com.

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

W. Vaccination providers will monitor and comply with CDC and/or emergency response stakeholder vaccine management requirements (e.g., requirements concerning obtaining, tracking, and handling vaccine) and with requirements concerning reporting of vaccine administration data to CDC.

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

<u>Conditions Related to Printed Matter, Advertising, and Promotion</u>

Y. All descriptive printed matter, advertising, and promotional material relating to the use of the Bivalent shall be consistent with the authorized labeling, as well as the terms set forth in this EUA, and meet the requirements set forth in Section 502(a) and (n) of the FD&C Act and FDA implementing regulations.

Z. All descriptive printed matter, advertising, and promotional material relating to the use of the Bivalent clearly and conspicuously shall state that:
- The Moderna COVID-19 Vaccine, Bivalent has not been approved or licensed by FDA, but has been authorized for emergency use by FDA, under an EUA to

prevent Coronavirus Disease 2019 (COVID-19) for use in individuals 6 months of age and older; and

- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of the medical product under Section 564(b)(1) of the FD&C Act unless the declaration is terminated or authorization revoked sooner.

Condition Related to Export

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

If the Moderna COVID-19 Vaccine is exported from the United States, conditions C, D, and P through Z do not apply, but export is permitted only if 1) the vaccine was manufactured on or before April 18, 2023, 2) the regulatory authorities of the country in which the vaccine will be used are fully informed that this vaccine is subject to an EUA and is not approved or licensed by FDA, 3) the intended use of the vaccine will comply in all respects with the laws of the country in which the product will be used, 4) the Fact Sheets that were authorized as of December 8, 2022 for the vial presentation being exported are made available, upon request, to the regulatory authorities of the countries in which the vaccine will be used, and 5) the regulatory authorities are informed that the Moderna COVID-19 Vaccine and associated Fact Sheets are no longer authorized for use in the United States and that FDA is not currently revising the Fact Sheets with updated information.

IV. Duration of Authorization

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

Sincerely,

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