FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE: EMERGENCY USE AUTHORIZATION OF PFIZER-BIONTECH 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 Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) under the EUA. See the FULL FACT SHEET FOR HEALTHCARE PROVIDERS for Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5).

Pfizer-BioNTech 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 Pfizer-BioNTech 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. (1)

The Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) is not licensed for any use. (1)

See Full Fact Sheet for Healthcare Providers for the justification for emergency use of Pfizer-BioNTech 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	Pfizer-BioNTech COVID-19 Vaccine, Bivalent Vial Cap and Label Border Color	Dosing Regimen, Dose and Schedule
6m-4y[1]	Maroon	3 doses, 0.2 mL each Dose 1: Week 0 Dose 2: Week 3 Dose 3: ≥ 8 weeks after Dose 2
5-11y	Orange	Single dose, 0.2 mL
12-64y	Gray	Single dose, 0.3 mL
≥65y	Gray	Single dose, 0.3 mL One additional dose, 0.3 mL, may be administered ≥4 months after first dose of an authorized bivalent COVID-19 vaccine

[1] Notwithstanding the age limitations for use of the vaccine, individuals turning from 4 to 5 years of age during the vaccination series should receive all doses with Pfizer-BioNTech COVID-19 Vaccine, Bivalent supplied in vials with maroon caps and labels with maroon borders.

Individuals 6 months through 4 years of age previously vaccinated with the monovalent Pfizer-BioNTech COVID-19 Vaccine[2] (2.3)

Age	Number of Previous Doses of Pfizer-BioNTech COVID-19 Vaccine	Pfizer-BioNTech COVID-19 Vaccine, Bivalent Vial Cap and Label Border Color	Dosing Regimen, Dose and Schedule
6m-4y	1 previous dose	Maroon	2 doses[3], 0.2 mL each Dose 1: 3 weeks after receipt of Pfizer-BioNTech COVID-19 Vaccine Dose 2: ≥8 weeks after Dose 1
6m-4y	2 previous doses	Maroon	Single dose, 0.2 mL ≥8 weeks after receipt of second dose of Pfizer-BioNTech COVID-19 Vaccine
6m-4y	3 previous doses	Maroon	Single dose, 0.2 mL ≥2 months after receipt of third dose of Pfizer-BioNTech COVID-19 Vaccine

[2] The monovalent Pfizer-BioNTech COVID-19 Vaccine is no longer authorized for use in the United States.
[3] Notwithstanding the age limitations for use of the vaccine, individuals turning from 4 to 5 years of age during the vaccination series should receive 2 doses with Pfizer-BioNTech COVID-19 Vaccine, Bivalent supplied in vials with maroon caps and labels with maroon borders.

Individuals 5 years of age and older previously vaccinated with 1 or more doses of a monovalent COVID-19 vaccine[4] (2.3)

Age	Pfizer-BioNTech COVID-19 Vaccine, Bivalent Vial Cap and Label Border Color	Dosing Regimen, Dose and Schedule
5-11y	Orange	Single dose, 0.2 mL ≥2 months after monovalent COVID-19 vaccine
12-64y	Gray	Single dose, 0.3 mL ≥2 months after monovalent COVID-19 vaccine
≥65y	Gray	Single dose, 0.3 mL ≥2 months after monovalent COVID-19 vaccine One additional dose, 0.3 mL, may be administered ≥4 months after first dose of an authorized bivalent COVID-19 vaccine

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

For individuals with certain kinds of immunocompromise[5] 5 years of age and older, a single additional age-appropriate dose of Pfizer-BioNTech 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 Pfizer-BioNTech COVID-19 Vaccine, Bivalent may be administered at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances.

[5] 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.

---------- DOSAGE FORMS AND STRENGTHS ----------

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

- Individuals 6 months through 4 years of age: vials with maroon caps and labels with maroon borders, a single dose is 0.2 mL. (3)
- Individuals 5 through 11 years of age: vials with orange caps and labels with orange borders, a single dose is 0.2 mL. (3)
- Individuals 12 years of age and older: vials with gray caps and labels with gray borders, a single dose is 0.3 mL. (3)

----------CONTRAINDICATIONS----------

Known history of a severe allergic reaction (e.g., anaphylaxis) to any component of Pfizer-BioNTech COVID-19 Vaccine or Pfizer-BioNTech 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 the Pfizer-BioNTech COVID-19 Vaccine, the observed risk is highest in males 12 through 17 years of age. (5.2)

---------- ADVERSE REACTIONS ----------

Solicited adverse reactions included:

- 6 months through 23 months of age:
  Injection site redness, swelling, and tenderness; decreased appetite, drowsiness, fever, irritability. (6.1)
- 2 years of age and older:
  Injection site pain, redness, and swelling; chills, diarrhea, fatigue, fever, headache, new or worsened joint pain, new or worsened muscle pain, vomiting. (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 Pfizer-BioNTech 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. The reports should include the words "Pfizer-BioNTech COVID19 Vaccine, Bivalent EUA" in the description section of the report. To the extent feasible, report adverse events to Pfizer 1-800-438-1985 or provide a copy of the VAERS form to Pfizer www.pfizersafetyreporting.com (6.3)

See FACT SHEET FOR RECIPIENTS AND CAREGIVERS.

TABLE OF CONTENTS*

* Sections or subsections omitted from the EUA are not listed

FULL FACT SHEET FOR HEALTHCARE PROVIDERS

1 EMERGENCY USE AUTHORIZATION

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for the emergency use of Pfizer-BioNTech 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.

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

Pfizer-BioNTech 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 use of EUA authority is justified, based on a determination that there is a public health emergency, or a significant potential for a public health emergency, that affects, or has a significant potential to affect, national security or the health and security of United States citizens living abroad, and that involves biological agent(s) or a disease or condition that may be attributable to such agent(s). Criteria for issuing an EUA include:

- The biological agent(s) can cause a serious or life-threatening disease or condition;

---

[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.").

- 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. COMIRNATY (COVID-19 Vaccine, mRNA) and SPIKEVAX (COVID-19 Vaccine, mRNA) are FDA-approved monovalent COVID-19 vaccines.

For information on clinical studies of Pfizer-BioNTech 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

- Pfizer-BioNTech COVID-19 Vaccine, Bivalent multiple dose vials and single dose vials contain a frozen suspension that does not contain a preservative and must be thawed prior to administration.
- There are 4 presentations of Pfizer-BioNTech COVID-19 Vaccine, Bivalent *[see Dosage and Administration (2.3)]*:
  - Multiple dose vials with maroon caps and labels with maroon borders. This presentation is authorized to provide doses for individuals 6 months through 4 years of age. Must be diluted.
  - Multiple dose vials with orange caps and labels with orange borders. This presentation is authorized to provide doses for individuals 5 through 11 years of age. Must be diluted.
  - Single dose vials with gray caps and labels with gray borders. This presentation is authorized to provide doses for individuals 12 years of age and older. Do not dilute
  - Multiple dose vials with gray caps and labels with gray borders. This presentation is authorized to provide doses for individuals 12 years of age and older. Do not dilute

Thawing Instructions

Thaw each vial before use following the instructions below:

Pfizer-BioNTech COVID-19 Vaccine, Bivalent Presentation	**Thawing in Refrigerator**
Multiple dose vials with maroon caps and labels with maroon borders	Thaw between 2°C to 8°C (35°F to 46°F) • A carton of 10 vials may take up to 2 hours to thaw.
Multiple dose vials with orange caps and labels with orange borders	Thaw between 2°C to 8°C (35°F to 46°F) • A carton of 10 vials may take up to 4 hours to thaw.
Single dose vials and multiple dose vials with gray caps and labels with gray borders	Thaw between 2°C to 8°C (35°F to 46°F). • A carton of 10 single dose vials may take up to 2 hours to thaw. • A carton of 10 multiple dose vials may take up to 6 hours to thaw.

Alternatively, thaw vials at room temperature [up to 25°C (77°F)] for 30 minutes.

Storage of Thawed Vials:

- Thawed vials may be stored at room temperature [up to 25°C (77°F)] for up to 12 hours prior to use.
- Thawed vials can be stored in the refrigerator between 2°C to 8°C (35°F to 46°F) for up to 10 weeks prior to use.
- Do not refreeze.

Preparation Instructions for Multiple Dose Vials with Maroon Caps or Orange Caps that **MUST BE DILUTED BEFORE USE:**

- Before dilution, invert vaccine vial gently 10 times. **Do not shake.**
- Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain opaque amorphous particles.
- Do not use if liquid is discolored or if other particles are observed.
- Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent.
- Add the appropriate amount of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial as follows:

Pfizer-BioNTech COVID-19 Vaccine, Bivalent Multiple Dose Vaccine Vial Cap and Label Color	**Amount of Sterile 0.9% Sodium Chloride Injection to Use as Diluent**
Maroon caps and labels with maroon borders	2.2 mL
Orange caps and labels with orange borders	1.3 mL

- Before removing the needle from the vial, equalize vial pressure by withdrawing air into the empty diluent syringe.
- Gently invert the vial containing the Pfizer-BioNTech COVID-19 Vaccine, Bivalent 10 times to mix.
- Do not shake.
- Inspect the vaccine in the vial.

- The vaccine will be a white to off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
- Record the date and time of dilution on the vial label.
- After dilution, multiple dose vials contain 10 doses of 0.2 mL each.
- Withdraw 0.2 mL of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent preferentially using low dead-volume syringes and/or needles. If standard syringes and needles are used, there may not be sufficient volume to extract 10 doses from a single vial.
- After dilution, the vial should be held between 2ºC to 25°C (35°F to 77°F). Vials should be discarded 12 hours after dilution.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.2 mL, discard the vial and any excess volume. Do not pool excess vaccine from multiple vials.

Preparation Instructions for Single Dose Vials and Multiple Dose Vials with Gray Caps and Labels with Gray Borders that **MUST NOT BE DILUTED**

- Prior to mixing, the thawed vaccine may contain white to off-white opaque amorphous particles.
- Before use, mix by inverting vaccine vial gently 10 times.
- Do not shake.
- After mixing, the vaccine should appear as a white to off-white suspension with no visible particles.
- Do not use if liquid is discolored or if particles are observed after mixing.

Single Dose Vials with Gray Caps and Labels with Gray Borders
- Withdraw a single 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent.
- Administer immediately.
- Discard vial and any excess volume.

Multiple Dose Vials with Gray Caps and Labels with Gray Borders
- Multiple dose vials contain 6 doses of 0.3 mL each.
- Withdraw 0.3 mL of the Pfizer-BioNTech COVID19 Vaccine, Bivalent preferentially using low dead-volume syringes and/or needles. If standard syringes and needles are used, there may not be sufficient volume to extract 6 doses from a single vial.
- Record the date and time of first vial puncture on the vial label.
- Store between 2°C to 25°C (35°F to 77°F).
- Discard any unused vaccine 12 hours after first puncture.
- If the amount of vaccine remaining in a multiple dose vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. Do not pool excess vaccine from multiple vials.

2.2 Administration

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The vaccine will be a white to off-white suspension. Do not administer if vaccine is discolored or contains particulate matter.
Administer Pfizer-BioNTech COVID-19 Vaccine, Bivalent intramuscularly.

2.3 Dose and Schedule

Individuals 6 months of age and older not previously vaccinated with a COVID-19 vaccine

Age	Pfizer-BioNTech COVID-19 Vaccine, Bivalent Vial Cap and Label Border Color	Dosing Regimen, Dose and Schedule
6m-4y[3]	Maroon	3 doses, 0.2 mL each Dose 1: Week 0 Dose 2: Week 3 Dose 3: ≥8 weeks after Dose 2
5-11y	Orange	Single dose, 0.2 mL
12-64y	Gray	Single dose, 0.3 mL
≥65y	Gray	Single dose, 0.3 mL One additional dose, 0.3 mL, may be administered ≥4 months after first dose of an authorized bivalent COVID-19 vaccine

Individuals 6 months through 4 years of age previously vaccinated with the monovalent Pfizer-BioNTech COVID-19 Vaccine[4]

Age	Number of Previous Doses of Pfizer-BioNTech COVID-19 Vaccine	Pfizer-BioNTech COVID-19 Vaccine, Bivalent Vial Cap and Label Border Color	Dosing Regimen, Dose and Schedule
6m-4y	1 previous dose	Maroon	2 doses[5], 0.2 mL each Dose 1: 3 weeks after receipt of Pfizer-BioNTech COVID-19 Vaccine Dose 2: ≥8 weeks after Dose 1
6m-4y	2 previous doses	Maroon	Single dose, 0.2 mL ≥8 weeks after receipt of second dose of Pfizer-BioNTech COVID-19 Vaccine
6m-4y	3 previous doses	Maroon	Single dose, 0.2 mL ≥2 months after receipt of third dose of Pfizer-BioNTech COVID-19 Vaccine

[3] Notwithstanding the age limitations for use of the vaccine, individuals turning from 4 to 5 years of age during the vaccination series should receive all doses with Pfizer-BioNTech COVID-19 Vaccine, Bivalent supplied in vials with maroon caps and labels with maroon borders.
[4] The monovalent Pfizer-BioNTech COVID-19 Vaccine is no longer authorized for use in the United States.
[5] Notwithstanding the age limitations for use of the vaccine, individuals turning from 4 to 5 years of age during the vaccination series should receive 2 doses with Pfizer-BioNTech COVID-19 Vaccine, Bivalent supplied in vials with maroon caps and labels with maroon borders.

Individuals 5 years of age and older previously vaccinated with 1 or more doses of a monovalent COVID-19 vaccine[6]

Age	Pfizer-BioNTech COVID-19 Vaccine, Bivalent Vial Cap and Label Border Color	Dosing Regimen, Dose and Schedule
5-11y	Orange	Single dose, 0.2 mL ≥2 months after monovalent COVID-19 vaccine
12-64y	Gray	Single dose, 0.3 mL ≥2 months after monovalent COVID-19 vaccine
≥65y	Gray	Single dose, 0.3 mL ≥2 months after monovalent COVID-19 vaccine One additional dose, 0.3 mL, may be administered ≥4 months after first dose of an authorized bivalent COVID-19 vaccine

For individuals with certain kinds of immunocompromise[7] 5 years of age and older, a single additional age-appropriate dose of Pfizer-BioNTech 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 Pfizer-BioNTech 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

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

Individuals 6 months through 4 years of age: vials with maroon caps and labels with maroon borders, a single dose is 0.2 mL.

Individuals 5 through 11 years of age: vials with orange caps and labels with orange borders, a single dose is 0.2 mL.

Individuals 12 years of age and older: vials with gray caps and labels with gray borders, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

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

[6] Monovalent refers to a COVID-19 vaccine that contains or encodes the spike protein of only the Original SARS-CoV-2.
[7] 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 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 Pfizer-BioNTech COVID-19 Vaccine, Bivalent.

Monitor Pfizer-BioNTech 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 Pfizer-BioNTech COVID-19 Vaccine are relevant to Pfizer-BioNTech 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 the Pfizer-BioNTech COVID-19 Vaccine, the observed risk is highest in males 12 through 17 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 Pfizer-BioNTech COVID-19 Vaccine, Bivalent.

5.5 Limitations of Vaccine Effectiveness

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

6 ADVERSE REACTIONS

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

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

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

Pfizer-BioNTech COVID-19 Vaccine

The safety of the primary series Pfizer-BioNTech COVID-19 Vaccine was evaluated in participants 6 months of age and older in 3 clinical studies conducted in the United States, Europe, Turkey, South Africa and South America.

Study BNT162-01 (Study 1) was a Phase 1/2, 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age. Study C4591001 (Study 2) is a Phase 1/2/3, multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose finding, vaccine candidate-selection (Phase 1) and efficacy (Phase 2/3) study that has enrolled approximately 46,000 participants, 12 years of age and older. Of these, approximately 43,448 participants [21,720 Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA); 21,728 placebo] in Phase 2/3 are 16 years of age or older (including 138 and 145 participants 16 and 17 years of age in the vaccine and placebo groups, respectively) and 2,260 participants are 12 through 15 years of age (1,131 and 1,129 in the vaccine and placebo groups, respectively). Study C4591007 (Study 3) is a Phase 1/2/3 multicenter, randomized, dose finding, open label (Phase 1) and multinational, saline placebo-controlled, observer-blind, immunogenicity and efficacy (Phase 2/3) study that has enrolled 4,695 participants 5 through 11 years of age, of whom 3,109 participants received Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) and 1,538 participants received placebo in Phase 2/3. Study 3 also enrolled 1,776 participants 6 through 23 months of age, of whom 1,178 participants were in the Pfizer-BioNTech COVID-19 Vaccine (3 mcg modRNA) group and 598 participants in the placebo group; and also enrolled 2,750 participants 2 through 4 years of age, of whom 1,835 participants were in the Pfizer-BioNTech COVID-19 Vaccine group and 915 participants in the placebo group in Phase 2/3.

In Study 2 and Study 3, all participants 6 months through 4 years of age, 5 through 11 years of age, 12 through 15 years of age, and a subset of participants 16 years of age and older, were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month after the last vaccination (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination].

Pfizer-BioNTech COVID-19 Vaccine Administered as a Primary Series

Participants 16 Years of Age and Older (2-Dose Primary Series)

At the time of the analysis of Study 2 for the EUA, 37,586 [18,801 Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) and 18,785 placebo] participants 16 years of age or older had been followed for a median of 2 months after the second dose.

The safety evaluation in Study 2 is ongoing. The safety population includes participants 16 years of age and older enrolled by October 9, 2020, and includes safety data accrued through November 14, 2020.

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received Pfizer-BioNTech COVID-19 Vaccine and those who received placebo. Overall, among the total participants who received either the Pfizer-BioNTech COVID-19 Vaccine or placebo, 50.6% were male and 49.4% were female, 83.1% were White, 9.1% were Black or African American, 28.0% were Hispanic/Latino, 4.3% were Asian, and 0.5% were American Indian/Alaska Native.

Solicited Local and Systemic Adverse Reactions

Across both age groups, 18 through 55 years of age and 56 years of age and older, the mean duration of pain at the injection site after Dose 2 was 2.5 days (range 1 to 36 days), for redness 2.6 days (range 1 to 34 days), and for swelling 2.3 days (range 1 to 34 days) for participants in the Pfizer-BioNTech COVID-19 Vaccine group.

Solicited reactogenicity data in 16 and 17 year-old participants are limited.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 18 Through 55 Years of Age‡ – Reactogenicity Subset of the Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=2291 n[b] (%)	**Placebo Dose 1 N[a]=2298 n[b] (%)**	**Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=2098 n[b] (%)**	**Placebo Dose 2 N[a]=2103 n[b] (%)**
Redness[c]				
Any (>2 cm)	104 (4.5)	26 (1.1)	123 (5.9)	14 (0.7)
Mild	70 (3.1)	16 (0.7)	73 (3.5)	8 (0.4)
Moderate	28 (1.2)	6 (0.3)	40 (1.9)	6 (0.3)
Severe	6 (0.3)	4 (0.2)	10 (0.5)	0 (0.0)
Swelling[c]				
Any (>2 cm)	132 (5.8)	11 (0.5)	132 (6.3)	5 (0.2)
Mild	88 (3.8)	3 (0.1)	80 (3.8)	3 (0.1)
Moderate	39 (1.7)	5 (0.2)	45 (2.1)	2 (0.1)
Severe	5 (0.2)	3 (0.1)	7 (0.3)	0 (0.0)

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=2291 n[b] (%)	Placebo Dose 1 N[a]=2298 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=2098 n[b] (%)	Placebo Dose 2 N[a]=2103 n[b] (%)
Pain at the injection site[d]				
Any	1904 (83.1)	322 (14.0)	1632 (77.8)	245 (11.7)
Mild	1170 (51.1)	308 (13.4)	1039 (49.5)	225 (10.7)
Moderate	710 (31.0)	12 (0.5)	568 (27.1)	20 (1.0)
Severe	24 (1.0)	2 (0.1)	25 (1.2)	0 (0.0)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.
‡ Eight participants were between 16 and 17 years of age.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 18 Through 55 Years of Age‡ – Reactogenicity Subset of the Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=2291 n[b] (%)	Placebo Dose 1 N[a]=2298 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=2098 n[b] (%)	Placebo Dose 2 N[a]=2103 n[b] (%)
Fever				
≥38.0°C	85 (3.7)	20 (0.9)	331 (15.8)	10 (0.5)
≥38.0°C to 38.4°C	64 (2.8)	10 (0.4)	194 (9.2)	5 (0.2)
>38.4°C to 38.9°C	15 (0.7)	5 (0.2)	110 (5.2)	3 (0.1)
>38.9°C to 40.0°C	6 (0.3)	3 (0.1)	26 (1.2)	2 (0.1)
>40.0°C	0 (0.0)	2 (0.1)	1 (0.0)	0 (0.0)
Fatigue[c]				
Any	1085 (47.4)	767 (33.4)	1247 (59.4)	479 (22.8)
Mild	597 (26.1)	467 (20.3)	442 (21.1)	248 (11.8)
Moderate	455 (19.9)	289 (12.6)	708 (33.7)	217 (10.3)
Severe	33 (1.4)	11 (0.5)	97 (4.6)	14 (0.7)
Headache[c]				
Any	959 (41.9)	775 (33.7)	1085 (51.7)	506 (24.1)
Mild	628 (27.4)	505 (22.0)	538 (25.6)	321 (15.3)
Moderate	308 (13.4)	251 (10.9)	480 (22.9)	170 (8.1)
Severe	23 (1.0)	19 (0.8)	67 (3.2)	15 (0.7)
Chills[c]				

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=2291 n[b] (%)	Placebo Dose 1 N[a]=2298 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=2098 n[b] (%)	Placebo Dose 2 N[a]=2103 n[b] (%)
Any	321 (14.0)	146 (6.4)	737 (35.1)	79 (3.8)
Mild	230 (10.0)	111 (4.8)	359 (17.1)	65 (3.1)
Moderate	82 (3.6)	33 (1.4)	333 (15.9)	14 (0.7)
Severe	9 (0.4)	2 (0.1)	45 (2.1)	0 (0.0)
Vomiting[d]				
Any	28 (1.2)	28 (1.2)	40 (1.9)	25 (1.2)
Mild	24 (1.0)	22 (1.0)	28 (1.3)	16 (0.8)
Moderate	4 (0.2)	5 (0.2)	8 (0.4)	9 (0.4)
Severe	0 (0.0)	1 (0.0)	4 (0.2)	0 (0.0)
Diarrhea[e]				
Any	255 (11.1)	270 (11.7)	219 (10.4)	177 (8.4)
Mild	206 (9.0)	217 (9.4)	179 (8.5)	144 (6.8)
Moderate	46 (2.0)	52 (2.3)	36 (1.7)	32 (1.5)
Severe	3 (0.1)	1 (0.0)	4 (0.2)	1 (0.0)
New or worsened muscle pain[c]				
Any	487 (21.3)	249 (10.8)	783 (37.3)	173 (8.2)
Mild	256 (11.2)	175 (7.6)	326 (15.5)	111 (5.3)
Moderate	218 (9.5)	72 (3.1)	410 (19.5)	59 (2.8)
Severe	13 (0.6)	2 (0.1)	47 (2.2)	3 (0.1)
New or worsened joint pain[c]				
Any	251 (11.0)	138 (6.0)	459 (21.9)	109 (5.2)
Mild	147 (6.4)	95 (4.1)	205 (9.8)	54 (2.6)
Moderate	99 (4.3)	43 (1.9)	234 (11.2)	51 (2.4)
Severe	5 (0.2)	0 (0.0)	20 (1.0)	4 (0.2)
Use of antipyretic or pain medication[f]	638 (27.8)	332 (14.4)	945 (45.0)	266 (12.6)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.
‡ Eight participants were between 16 and 17 years of age.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1802 n[b] (%)	Placebo Dose 1 N[a]=1792 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1660 n[b] (%)	Placebo Dose 2 N[a]=1646 n[b] (%)
Redness[c]				
Any (>2 cm)	85 (4.7)	19 (1.1)	120 (7.2)	12 (0.7)
Mild	55 (3.1)	12 (0.7)	59 (3.6)	8 (0.5)
Moderate	27 (1.5)	5 (0.3)	53 (3.2)	3 (0.2)
Severe	3 (0.2)	2 (0.1)	8 (0.5)	1 (0.1)
Swelling[c]				
Any (>2 cm)	118 (6.5)	21 (1.2)	124 (7.5)	11 (0.7)
Mild	71 (3.9)	10 (0.6)	68 (4.1)	5 (0.3)
Moderate	45 (2.5)	11 (0.6)	53 (3.2)	5 (0.3)
Severe	2 (0.1)	0 (0.0)	3 (0.2)	1 (0.1)
Pain at the injection site[d]				
Any (>2 cm)	1282 (71.1)	166 (9.3)	1098 (66.1)	127 (7.7)
Mild	1008 (55.9)	160 (8.9)	792 (47.7)	125 (7.6)
Moderate	270 (15.0)	6 (0.3)	298 (18.0)	2 (0.1)
Severe	4 (0.2)	0 (0.0)	8 (0.5)	0 (0.0)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1802 n[b] (%)	Placebo Dose 1 N[a]=1792 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1660 n[b] (%)	Placebo Dose 2 N[a]=1646 n[b] (%)
Fever				
≥38.0°C	26 (1.4)	7 (0.4)	181 (10.9)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.3)	2 (0.1)	131 (7.9)	2 (0.1)
>38.4°C to 38.9°C	1 (0.1)	3 (0.2)	45 (2.7)	1 (0.1)
>38.9°C to 40.0°C	1 (0.1)	2 (0.1)	5 (0.3)	1 (0.1)
>40.0°C	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue[c]				
Any	615 (34.1)	405 (22.6)	839 (50.5)	277 (16.8)
Mild	373 (20.7)	252 (14.1)	351 (21.1)	161 (9.8)
Moderate	240 (13.3)	150 (8.4)	442 (26.6)	114 (6.9)

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1802 n[b] (%)	Placebo Dose 1 N[a]=1792 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1660 n[b] (%)	Placebo Dose 2 N[a]=1646 n[b] (%)
Severe	2 (0.1)	3 (0.2)	46 (2.8)	2 (0.1)
Headache[c]				
Any	454 (25.2)	325 (18.1)	647 (39.0)	229 (13.9)
Mild	348 (19.3)	242 (13.5)	422 (25.4)	165 (10.0)
Moderate	104 (5.8)	80 (4.5)	216 (13.0)	60 (3.6)
Severe	2 (0.1)	3 (0.2)	9 (0.5)	4 (0.2)
Chills[c]				
Any	113 (6.3)	57 (3.2)	377 (22.7)	46 (2.8)
Mild	87 (4.8)	40 (2.2)	199 (12.0)	35 (2.1)
Moderate	26 (1.4)	16 (0.9)	161 (9.7)	11 (0.7)
Severe	0 (0.0)	1 (0.1)	17 (1.0)	0 (0.0)
Vomiting[d]				
Any	9 (0.5)	9 (0.5)	11 (0.7)	5 (0.3)
Mild	8 (0.4)	9 (0.5)	9 (0.5)	5 (0.3)
Moderate	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
Diarrhea[e]				
Any	147 (8.2)	118 (6.6)	137 (8.3)	99 (6.0)
Mild	118 (6.5)	100 (5.6)	114 (6.9)	73 (4.4)
Moderate	26 (1.4)	17 (0.9)	21 (1.3)	22 (1.3)
Severe	3 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[c]				
Any	251 (13.9)	149 (8.3)	477 (28.7)	87 (5.3)
Mild	168 (9.3)	100 (5.6)	202 (12.2)	57 (3.5)
Moderate	82 (4.6)	46 (2.6)	259 (15.6)	29 (1.8)
Severe	1 (0.1)	3 (0.2)	16 (1.0)	1 (0.1)
New or worsened joint pain[c]				
Any	155 (8.6)	109 (6.1)	313 (18.9)	61 (3.7)
Mild	101 (5.6)	68 (3.8)	161 (9.7)	35 (2.1)
Moderate	52 (2.9)	40 (2.2)	145 (8.7)	25 (1.5)
Severe	2 (0.1)	1 (0.1)	7 (0.4)	1 (0.1)
Use of antipyretic or pain medication	358 (19.9)	213 (11.9)	625 (37.7)	161 (9.8)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

Unsolicited Adverse Events

Serious Adverse Events
In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (Pfizer-BioNTech COVID-19 Vaccine = 10,841; placebo = 10,851), serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported by 0.4% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 0.3% of placebo recipients. In a similar analysis, in participants 56 years of age and older (Pfizer-BioNTech COVID-19 Vaccine = 7,960, placebo = 7,934), serious adverse events were reported by 0.8% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 0.6% of placebo recipients who received at least 1 dose of Pfizer-BioNTech COVID-19 Vaccine or placebo, respectively. In these analyses, 91.6% of study participants had at least 30 days of follow-up after Dose 2.

Appendicitis was reported as a serious adverse event for 12 participants, and numerically higher in the vaccine group, 8 vaccine participants and 4 placebo participants. 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 serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Non-Serious Adverse Events
In Study 2 in which 10,841 participants 16 through 55 years of age received Pfizer-BioNTech COVID-19 Vaccine and 10,851 participants received placebo, non-serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported in 29.3% of participants who received Pfizer-BioNTech COVID-19 Vaccine and 13.2% of participants in the placebo group, for participants who received at least 1 dose. Overall, in a similar analysis in which 7,960 participants 56 years of age and older received Pfizer-BioNTech COVID-19 Vaccine, non-serious adverse events within 30 days were reported in 23.8% of participants who received Pfizer-BioNTech COVID-19 Vaccine and 11.7% of participants in the placebo group, for participants who received at least 1 dose. In these analyses, 91.6% of study participants had at least 30 days of follow-up after Dose 2.

The higher frequency of reported unsolicited non-serious adverse events among Pfizer-BioNTech COVID-19 Vaccine recipients compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following vaccination that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Tables 3 and 4. From Dose 1 through 30 days after Dose 2, reports of lymphadenopathy were imbalanced with notably more cases in the Pfizer-BioNTech COVID-19 Vaccine group (64) vs. the placebo group (6), which is plausibly related to vaccination. Throughout the safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the Pfizer-BioNTech COVID-19 Vaccine group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. No cases of Bell's palsy were reported in the placebo group. 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 non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Participants 12 Through 15 Years of Age (2-Dose Primary Series)

In an analysis of Study 2, based on data up to the cutoff date of March 13, 2021, 2,260 participants (1,131 Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA); 1,129 placebo) were 12 through 15 years of age. Of these, 1,308 (660 Pfizer-BioNTech COVID-19 Vaccine and 648 placebo) participants have been followed for at least 2 months after the second dose. The safety evaluation in Study 2 is ongoing.

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received Pfizer-BioNTech COVID-19 Vaccine and those who received placebo. Overall, among the participants who received the Pfizer-BioNTech COVID-19 Vaccine, 50.1% were male and 49.9% were female, 85.9% were White, 4.6% were Black or African American, 11.7% were Hispanic/Latino, 6.4% were Asian, and 0.4% were American Indian/Alaska Native.

Solicited Local and Systemic Adverse Reactions

The mean duration of pain at the injection site after Dose 1 was 2.4 days (range 1 to 10 days), for redness 2.4 days (range 1 to 16 days), and for swelling 1.9 days (range 1 to 5 days) for participants in the Pfizer-BioNTech COVID-19 Vaccine group.

Table 5: Study 2 – Frequency and Percentages of Participants With Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 12 Through 15 Years of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1127 n[b] (%)	**Placebo Dose 1 N[a]=1127 n[b] (%)**	**Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1097 n[b] (%)**	**Placebo Dose 2 N[a]=1078 n[b] (%)**
Redness[c]				
Any (>2 cm)	65 (5.8)	12 (1.1)	55 (5.0)	10 (0.9)
Mild	44 (3.9)	11 (1.0)	29 (2.6)	8 (0.7)
Moderate	20 (1.8)	1 (0.1)	26 (2.4)	2 (0.2)
Severe	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Swelling[c]				
Any (>2 cm)	78 (6.9)	11 (1.0)	54 (4.9)	6 (0.6)
Mild	55 (4.9)	9 (0.8)	36 (3.3)	4 (0.4)
Moderate	23 (2.0)	2 (0.2)	18 (1.6)	2 (0.2)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pain at the injection site[d]				
Any	971 (86.2)	263 (23.3)	866 (78.9)	193 (17.9)
Mild	467 (41.4)	227 (20.1)	466 (42.5)	164 (15.2)
Moderate	493 (43.7)	36 (3.2)	393 (35.8)	29 (2.7)
Severe	11 (1.0)	0 (0.0)	7 (0.6)	0 (0.0)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1127 n[b] (%)	Placebo Dose 1 N[a]=1127 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1097 n[b] (%)	Placebo Dose 2 N[a]=1078 n[b] (%)

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

Table 6: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 12 Through 15 Years of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1127 n[b] (%)	Placebo Dose 1 N[a]=1127 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1097 n[b] (%)	Placebo Dose 2 N[a]=1078 n[b] (%)
Fever				
≥38.0°C	114 (10.1)	12 (1.1)	215 (19.6)	7 (0.6)
≥38.0°C to 38.4°C	74 (6.6)	8 (0.7)	107 (9.8)	5 (0.5)
>38.4°C to 38.9°C	29 (2.6)	2 (0.2)	83 (7.6)	1 (0.1)
>38.9°C to 40.0°C	10 (0.9)	2 (0.2)	25 (2.3)	1 (0.1)
>40.0°C	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue[c]				
Any	677 (60.1)	457 (40.6)	726 (66.2)	264 (24.5)
Mild	278 (24.7)	250 (22.2)	232 (21.1)	133 (12.3)
Moderate	384 (34.1)	199 (17.7)	468 (42.7)	127 (11.8)
Severe	15 (1.3)	8 (0.7)	26 (2.4)	4 (0.4)
Headache[c]				
Any	623 (55.3)	396 (35.1)	708 (64.5)	263 (24.4)
Mild	361 (32.0)	256 (22.7)	302 (27.5)	169 (15.7)
Moderate	251 (22.3)	131 (11.6)	384 (35.0)	93 (8.6)
Severe	11 (1.0)	9 (0.8)	22 (2.0)	1 (0.1)
Chills[c]				
Any	311 (27.6)	109 (9.7)	455 (41.5)	73 (6.8)
Mild	195 (17.3)	82 (7.3)	221 (20.1)	52 (4.8)
Moderate	111 (9.8)	25 (2.2)	214 (19.5)	21 (1.9)
Severe	5 (0.4)	2 (0.2)	20 (1.8)	0 (0.0)
Vomiting[d]				
Any	31 (2.8)	10 (0.9)	29 (2.6)	12 (1.1)
Mild	30 (2.7)	8 (0.7)	25 (2.3)	11 (1.0)
Moderate	0 (0.0)	2 (0.2)	4 (0.4)	1 (0.1)
Severe	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1127 n[b] (%)	Placebo Dose 1 N[a]=1127 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1097 n[b] (%)	Placebo Dose 2 N[a]=1078 n[b] (%)
Diarrhea[e]				
Any	90 (8.0)	82 (7.3)	65 (5.9)	43 (4.0)
Mild	77 (6.8)	72 (6.4)	59 (5.4)	38 (3.5)
Moderate	13 (1.2)	10 (0.9)	6 (0.5)	5 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
New or worsened muscle pain[c]				
Any	272 (24.1)	148 (13.1)	355 (32.4)	90 (8.3)
Mild	125 (11.1)	88 (7.8)	152 (13.9)	51 (4.7)
Moderate	145 (12.9)	60 (5.3)	197 (18.0)	37 (3.4)
Severe	2 (0.2)	0 (0.0)	6 (0.5)	2 (0.2)
New or worsened joint pain[c]				
Any	109 (9.7)	77 (6.8)	173 (15.8)	51 (4.7)
Mild	66 (5.9)	50 (4.4)	91 (8.3)	30 (2.8)
Moderate	42 (3.7)	27 (2.4)	78 (7.1)	21 (1.9)
Severe	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)
Use of antipyretic or pain medication[f]	413 (36.6)	111 (9.8)	557 (50.8)	95 (8.8)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.
* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.
± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

Unsolicited Adverse Events

In the following analyses of Study 2 in participants 12 through 15 years of age (1,131 of whom received Pfizer-BioNTech COVID-19 Vaccine and 1,129 of whom received placebo), 98.3% of study participants had at least 30 days of follow-up after Dose 2.

Serious Adverse Events

Serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported by 0.4% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 0.1% of placebo recipients. There were no notable patterns or numerical imbalances between treatment groups for specific categories of serious adverse events that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Non-Serious Adverse Events
Non-serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported by 5.8% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 5.8% of placebo recipients. From Dose 1 through 30 days after Dose 2, reports of lymphadenopathy plausibly related to the study intervention were imbalanced, with notably more cases in the Pfizer-BioNTech COVID-19 Vaccine group (7) vs. the placebo group (1). There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Participants 5 Through 11 Years of Age (2-Dose Primary Series)

In an analysis of Study 3 Phase 2/3, based on data up to the cutoff date of September 06, 2021, 2,268 participants [1,518 Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA); 750 placebo] were 5 through 11 years of age. Of these, 2,158 (95.1%) [1,444 Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) and 714 placebo] participants have been followed for at least 2 months after the second dose. An analysis of Study 3 Phase 2/3 adverse event data also included another 2,379 participants [1,591 Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) and 788 placebo], of whom 71.2% had a follow-up period for at least 2 weeks after Dose 2 up to the cutoff date of October 8, 2021. The safety evaluation in Study 3 is ongoing.

Demographic characteristics in Study 3 were generally similar with regard to age, gender, race, and ethnicity among participants 5 through 11 years of age who received Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) and those who received placebo. Among the 4,647 participants 5 through 11 years of age who received at least 1 dose of the Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) or placebo, 51.8% were male and 48.2% were female, 77.3% were White, 5.8% were Black or African American, 16.9% were Hispanic/Latino, 8.3% were Asian, and 0.4% were American Indian/Alaska Native.

Solicited Local and Systemic Adverse Reactions

The mean duration of pain at the injection site after Dose 2 was 2.3 days (range 1 to 11 days), for redness 2.2 days (range 1 to 10 days), and for swelling 2.2 days (range 1 to 10 days) for children in the Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) group up to the cutoff date of September 06, 2021.

Table 7: Study 3 – Frequency and Percentages of Participants With Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Children 5 Through 11 Years of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1511 n[c] (%)	**Placebo Dose 1 N[a,b]=748 n[c] (%)**	**Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1501 n[c] (%)**	**Placebo Dose 2 N[a,b]=740 n[c] (%)**
Redness[d]				
Any (≥0.5 cm)	222 (14.7)	43 (5.7)	278 (18.5)	40 (5.4)
Mild	143 (9.5)	37 (4.9)	143 (9.5)	31 (4.2)
Moderate	79 (5.2)	6 (0.8)	132 (8.8)	9 (1.2)
Severe	0	0	3 (0.2)	0

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1511 n[c] (%)	Placebo Dose 1 N[a,b]=748 n[c] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1501 n[c] (%)	Placebo Dose 2 N[a,b]=740 n[c] (%)
Swelling[d]				
Any (≥0.5 cm)	158 (10.5)	20 (2.7)	229 (15.3)	20 (2.7)
Mild	85 (5.6)	13 (1.7)	117 (7.8)	15 (2.0)
Moderate	72 (4.8)	7 (0.9)	112 (7.5)	5 (0.7)
Severe	1 (0.1)	0	0	0
Pain at the injection site[e]				
Any	1119 (74.1)	234 (31.3)	1065 (71.0)	218 (29.5)
Mild	890 (58.9)	204 (27.3)	793 (52.8)	192 (25.9)
Moderate	225 (14.9)	30 (4.0)	267 (17.8)	26 (3.5)
Severe	4 (0.3)	0	5 (0.3)	0

Note: Reactions were collected in an electronic diary (e-diary) from Day 1 to Day 7 after vaccination.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. The denominators (N) used in the percentage calculations for redness and swelling were 749 after Dose 1 and 741 after Dose 2 in the placebo group, due to an e-diary error.
c. n = Number of participants with the specified reaction.
d. Mild: ≥0.5 to ≤2.0 cm; Moderate: >2.0 to ≤7.0 cm; Severe: >7.0 cm.
e. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

* Randomized participants who received at least 1 dose of the study intervention.
± Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA).

Table 8: Study 3 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Children 5 Through 11 Years of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1511 n[c] (%)	Placebo Dose 1 N[a,b]=748 n[c] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1501 n[c] (%)	Placebo Dose 2 N[a,b]=740 n[c] (%)
Fever				
≥38.0°C	38 (2.5)	10 (1.3)	98 (6.5)	9 (1.2)
≥38.0°C to 38.4°C	23 (1.5)	4 (0.5)	51 (3.4)	5 (0.7)
>38.4°C to 38.9°C	12 (0.8)	5 (0.7)	38 (2.5)	3 (0.4)
>38.9°C to 40.0°C	3 (0.2)	1 (0.1)	8 (0.5)	1 (0.1)
>40.0°C	0	0	1 (0.1)	0
Fatigue[d]				
Any	508 (33.6)	234 (31.3)	592 (39.4)	180 (24.3)
Mild	333 (22.0)	150 (20.1)	321 (21.4)	96 (13.0)
Moderate	171 (11.3)	83 (11.1)	260 (17.3)	83 (11.2)
Severe	4 (0.3)	1 (0.1)	11 (0.7)	1 (0.1)
Headache[d]				
Any	339 (22.4)	180 (24.1)	420 (28.0)	138 (18.6)
Mild	249 (16.5)	131 (17.5)	281 (18.7)	93 (12.6)
Moderate	88 (5.8)	45 (6.0)	136 (9.1)	45 (6.1)

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1511 n[c] (%)	Placebo Dose 1 N[a,b]=748 n[c] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1501 n[c] (%)	Placebo Dose 2 N[a,b]=740 n[c] (%)
Severe	2 (0.1)	4 (0.5)	3 (0.2)	0
Chills[d]				
Any	70 (4.6)	35 (4.7)	147 (9.8)	32 (4.3)
Mild	54 (3.6)	30 (4.0)	105 (7.0)	24 (3.2)
Moderate	16 (1.1)	5 (0.7)	40 (2.7)	7 (0.9)
Severe	0	0	2 (0.1)	1 (0.1)
Vomiting[e]				
Any	33 (2.2)	11 (1.5)	28 (1.9)	6 (0.8)
Mild	26 (1.7)	11 (1.5)	27 (1.8)	6 (0.8)
Moderate	7 (0.5)	0	1 (0.1)	0
Severe	0	0	0	0
Diarrhea[f]				
Any	89 (5.9)	31 (4.1)	79 (5.3)	35 (4.7)
Mild	79 (5.2)	31 (4.1)	72 (4.8)	32 (4.3)
Moderate	10 (0.7)	0	7 (0.5)	3 (0.4)
Severe	0	0	0	0
New or worsened muscle pain[d]				
Any	137 (9.1)	51 (6.8)	175 (11.7)	55 (7.4)
Mild	96 (6.4)	35 (4.7)	116 (7.7)	38 (5.1)
Moderate	40 (2.6)	16 (2.1)	58 (3.9)	17 (2.3)
Severe	1 (0.1)	0	1 (0.1)	0
New or worsened joint pain[d]				
Any	50 (3.3)	41 (5.5)	78 (5.2)	27 (3.6)
Mild	34 (2.3)	31 (4.1)	57 (3.8)	20 (2.7)
Moderate	16 (1.1)	10 (1.3)	21 (1.4)	7 (0.9)
Severe	0	0	0	0
Use of antipyretic or pain medication[g]	217 (14.4)	62 (8.3)	296 (19.7)	60 (8.1)

Note: Events and use of antipyretic or pain medication were collected in an electronic diary (e-diary) from Day 1 to Day 7 after each dose.

a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. The denominators (N) used in the percentage calculations for fever and use of antipyretic or pain medication were 749 after Dose 1 and 741 after Dose 2 in the placebo group, due to an e-diary error.
c. n = Number of participants with the specified reaction.
d. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.
e. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.
f. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
g. Severity was not collected for use of antipyretic or pain medication.
* Randomized participants who received at least 1 dose of the study intervention.
± Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA).

Unsolicited Adverse Events

In the following analyses of Study 3 in children 5 through 11 years of age (1,518 of whom received Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) and 750 of whom received placebo), 99.5% of participants had at least 30 days of follow-up after Dose 2.

Serious Adverse Events
In 1 group of participants (initial enrollment cohort) with a median of 2.3 months follow-up post Dose 2, no serious adverse events were reported that were considered related to vaccination. In a second group of participants (expansion cohort) with a median of 2.4 weeks follow-up post Dose 2, no serious adverse events were reported that were considered related to vaccination.

Non-Serious Adverse Events
In 1 group of participants (initial enrollment cohort), non-serious adverse events from Dose 1 through up to 30 days after Dose 2 up to the cutoff date of September 06, 2021, in ongoing follow up were reported by 10.9% of Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) recipients and by 9.1% of placebo recipients. In this group of participants, >99% had follow-up 30 days post Dose 2. In a second group of participants (expansion cohort) for which the median follow-up was 2.4 weeks (range 0 to 3.7 weeks), non-serious adverse events from Dose 1 through the cutoff date of October 08, 2021, were reported by 7.1% of Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) recipients and by 6.3% of placebo recipients.

In the initial enrollment cohort, from Dose 1 through 30 days after Dose 2, lymphadenopathy was reported in 13 (0.9%) participants in the Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) group vs. 1 (0.1%) in the placebo group. In the expansion cohort from Dose 1 through the cutoff date, lymphadenopathy was reported in 6 (0.4%) participants in the Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) group vs. 3 (0.4%) in the placebo group. There were no other notable patterns between treatment groups for specific categories of non-serious adverse events that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Participants 2 Through 4 Years of Age (3-Dose Primary Series)

In an analysis of Study 3 (Phase 2/3), based on data in the blinded placebo-controlled follow-up period up to the cutoff date of April 29, 2022, 886 participants 2 through 4 years of age who received a 3-dose primary series [606 Pfizer-BioNTech COVID-19 Vaccine (3 mcg modRNA); 280 placebo] have been followed a median of 1.4 months after the third dose.

Demographic characteristics in Study 3 were generally similar with regard to age, gender, race, and ethnicity among participants 2 through 4 years of age who received Pfizer-BioNTech COVID-19 Vaccine and those who received placebo. Among the 1,835 participants 2 through 4 years of age who received at least 1 dose of the Pfizer-BioNTech COVID-19 Vaccine, 49.1% were male and 50.9% were female, 80.1% were White, 14.4% were Hispanic/Latino, 7.1% were multi-racial, 6.9% were Asian, 5.1% were Black or African American, and 0.2% were American Indian/Alaska Native.

Solicited Local and Systemic Adverse Reactions

The mean duration of pain at the injection site after Dose 3 was 1.7 days (range 1 to 14 days), for redness 1.5 days (range 1 to 3 days), and for swelling 1.8 days (range 1 to 4 days) for participants

2 through 4 years of age in the Pfizer-BioNTech COVID-19 Vaccine group in the blinded placebo-controlled follow-up period (cutoff date of April 29, 2022).

Table 9: Study 3 – Frequency and Percentages of Participants With Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 2 Through 4 Years of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1814 to 1825 n[b] (%)	Placebo Dose 1 N[a]=905 to 909 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1772 to 1779 n[b] (%)	Placebo Dose 2 N[a]=877 to 878 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 3 N[a]=547 to 552 n[b] (%)	Placebo Dose 3 N[a]=262 n[b] (%)
Redness[c]						
Any (≥0.5 cm)	160 (8.8)	77 (8.5)	202 (11.4)	50 (5.7)	60 (10.9)	9 (3.4)
Mild	137 (7.5)	67 (7.4)	170 (9.6)	43 (4.9)	53 (9.6)	7 (2.7)
Moderate	22 (1.2)	9 (1.0)	31 (1.7)	7 (0.8)	7 (1.3)	2 (0.8)
Severe	1 (0.1)	1 (0.1)	1 (0.1)	0	0	0
Swelling[c]						
Any (≥0.5 cm)	67 (3.7)	26 (2.9)	102 (5.7)	18 (2.1)	17 (3.1)	3 (1.1)
Mild	59 (3.2)	21 (2.3)	81 (4.6)	16 (1.8)	16 (2.9)	3 (1.1)
Moderate	8 (0.4)	5 (0.6)	21 (1.2)	2 (0.2)	1 (0.2)	0
Severe	0	0	0	0	0	0
Pain at the injection site[d]						
Any	559 (30.8)	186 (20.6)	550 (31.0)	178 (20.3)	146 (26.7)	35 (13.4)
Mild	522 (28.8)	178 (19.7)	514 (29.0)	169 (19.3)	130 (23.8)	33 (12.6)
Moderate	37 (2.0)	7 (0.8)	36 (2.0)	8 (0.9)	16 (2.9)	2 (0.8)
Severe	0	1 (0.1)	0	1 (0.1)	0	0

* Randomized participants who received at least 1 dose of the study intervention.
± Pfizer-BioNTech COVID-19 Vaccine (3 mcg modRNA).
Note: Reactions were collected in an electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: ≥0.5 to ≤2.0 cm; Moderate: >2.0 to ≤7.0 cm; Severe: >7.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 10: Study 3 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 2 Through 4 Years of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1813 to 1824 n[b] (%)	Placebo Dose 1 N[a]=905 to 909 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1772 to 1779 n[b] (%)	Placebo Dose 2 N[a]=877 to 878 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 3 N[a]=547 to 552 n[b] (%)	Placebo Dose 3 N[a]=262 n[b] (%)
Fever						
≥38.0°C	95 (5.2)	48 (5.3)	88 (4.9)	46 (5.2)	28 (5.1)	11 (4.2)
≥38.0°C to 38.4°C	57 (3.1)	24 (2.6)	41 (2.3)	17 (1.9)	16 (2.9)	4 (1.5)
>38.4°C to 38.9°C	24 (1.3)	16 (1.8)	26 (1.5)	21 (2.4)	8 (1.4)	4 (1.5)
>38.9°C to 40.0°C	13 (0.7)	8 (0.9)	19 (1.1)	8 (0.9)	4 (0.7)	3 (1.1)
>40.0°C	1 (0.1)	0	2 (0.1)	0	0	0
Fatigue[c]						
Any	539 (29.7)	277 (30.6)	456 (25.7)	201 (22.9)	134 (24.5)	57 (21.8)
Mild	335 (18.5)	176 (19.4)	267 (15.1)	120 (13.7)	87 (15.9)	35 (13.4)
Moderate	198 (10.9)	96 (10.6)	181 (10.2)	78 (8.9)	45 (8.2)	22 (8.4)
Severe	6 (0.3)	5 (0.6)	8 (0.5)	3 (0.3)	2 (0.4)	0
Headache[c]						
Any	81 (4.5)	44 (4.9)	81 (4.6)	36 (4.1)	27 (4.9)	11 (4.2)
Mild	63 (3.5)	35 (3.9)	63 (3.6)	23 (2.6)	19 (3.5)	10 (3.8)
Moderate	18 (1.0)	8 (0.9)	18 (1.0)	12 (1.4)	8 (1.5)	1 (0.4)
Severe	0	1 (0.1)	0	1 (0.1)	0	0
Chills[c]						
Any	41 (2.3)	22 (2.4)	53 (3.0)	23 (2.6)	18 (3.3)	7 (2.7)
Mild	28 (1.5)	16 (1.8)	35 (2.0)	17 (1.9)	14 (2.6)	7 (2.7)
Moderate	10 (0.6)	6 (0.7)	18 (1.0)	6 (0.7)	3 (0.5)	0
Severe	3 (0.2)	0	0	0	1 (0.2)	0
Vomiting[d]						
Any	54 (3.0)	24 (2.7)	61 (3.4)	29 (3.3)	9 (1.6)	10 (3.8)
Mild	44 (2.4)	14 (1.5)	55 (3.1)	26 (3.0)	7 (1.3)	9 (3.4)
Moderate	10 (0.6)	10 (1.1)	6 (0.3)	3 (0.3)	2 (0.4)	1 (0.4)
Severe	0	0	0	0	0	0
Diarrhea[e]						
Any	139 (7.7)	72 (8.0)	118 (6.7)	64 (7.3)	28 (5.1)	13 (5.0)
Mild	130 (7.2)	64 (7.1)	105 (5.9)	57 (6.5)	21 (3.8)	10 (3.8)
Moderate	9 (0.5)	8 (0.9)	12 (0.7)	7 (0.8)	7 (1.3)	3 (1.1)
Severe	0	0	1 (0.1)	0	0	0

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1813 to 1824 n[b] (%)	Placebo Dose 1 N[a]=905 to 909 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1772 to 1779 n[b] (%)	Placebo Dose 2 N[a]=877 to 878 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 3 N[a]=547 to 552 n[b] (%)	Placebo Dose 3 N[a]=262 n[b] (%)
New or worsened muscle pain[c]						
Any	43 (2.4)	15 (1.7)	46 (2.6)	21 (2.4)	11 (2.0)	4 (1.5)
Mild	33 (1.8)	13 (1.4)	33 (1.9)	17 (1.9)	8 (1.5)	4 (1.5)
Moderate	9 (0.5)	2 (0.2)	13 (0.7)	4 (0.5)	3 (0.5)	0
Severe	1 (0.1)	0	0	0	0	0
New or worsened joint pain[c]						
Any	14 (0.8)	18 (2.0)	24 (1.4)	9 (1.0)	7 (1.3)	2 (0.8)
Mild	12 (0.7)	13 (1.4)	18 (1.0)	6 (0.7)	5 (0.9)	2 (0.8)
Moderate	2 (0.1)	5 (0.6)	6 (0.3)	3 (0.3)	1 (0.2)	0
Severe	0	0	0	0	1 (0.2)	0
Use of antipyretic or pain medication[f]	197 (10.8)	83 (9.1)	177 (9.9)	74 (8.4)	47 (8.5)	18 (6.9)

* Randomized participants who received at least 1 dose of the study intervention.
± Pfizer-BioNTech COVID-19 Vaccine (3 mcg modRNA).
Note: Events and use of antipyretic or pain medication were collected in an electronic diary (e-diary) from Day 1 to Day 7 after each dose.
a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

In the following analyses of Study 3 in participants 2 through 4 years of age (606 of whom received Pfizer-BioNTech COVID-19 Vaccine and 280 of whom received placebo), 76.6% of participants had at least 30 days of follow-up after Dose 3.

Serious Adverse Events
Serious adverse events from Dose 1 through 1 month after Dose 3, with an overall median of 1.4 months follow-up after Dose 3 were reported by 0.7% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 0.9% of placebo recipients. One serious adverse event of fever (maximum temperature 40.3°C) on Day 3 after Dose 2 in a 4-year-old was considered possibly related to vaccination.

Non-Serious Adverse Events
Non-serious adverse events from Dose 1 through up to 30 days after Dose 3, in ongoing follow-up were reported by 18.5% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 18.5% of placebo recipients.

From Dose 1 through 30 days after Dose 3, lymphadenopathy was reported in 1 (0.1%) participant in the Pfizer-BioNTech COVID-19 Vaccine (3 mcg modRNA) group vs. 0 (0.0%) in the placebo group. There were no other notable patterns between treatment groups for specific categories of non-serious adverse events that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Participants 6 Through 23 Months of Age (3-Dose Primary Series)

In an analysis of Study 3 (Phase 2/3), based on data in the blinded placebo-controlled follow-up period up to the cutoff date of April 29, 2022, 570 participants 6 through 23 months of age who received a 3-dose primary series [386 Pfizer-BioNTech COVID-19 Vaccine (3 mcg modRNA); 184 placebo] have been followed for a median of 1.3 months after the third dose.

Demographic characteristics in Study 3 were generally similar with regard to age, gender, race, and ethnicity among participants 6 through 23 months of age who received Pfizer-BioNTech COVID-19 Vaccine and those who received placebo. Among the 1,178 participants 6 through 23 months of age who received at least 1 dose of the Pfizer-BioNTech COVID-19 Vaccine, 50.0% were male and 50.0% were female, 78.3% were White, 9.9% were multi-racial, 13.7% were Hispanic/Latino, 7.7% were Asian, 3.6% were Black or African American, and 0.3% were American Indian/Alaska Native.

Solicited Local and Systemic Adverse Reactions

The mean duration of tenderness at the injection site after Dose 3 was 1.5 days (range 1 to 9 days), for redness 1.5 days (range 1 to 5 days), and for swelling 1.8 days (range 1 to 3 days) for participants 6 through 23 months of age in the Pfizer-BioNTech COVID-19 Vaccine group in the blinded placebo-controlled follow-up period (cutoff date of April 29, 2022).

Table 11: Study 3 – Frequency and Percentages of Participants With Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 6 Through 23 Months of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1159 to 1173 n[b] (%)	**Placebo Dose 1 N[a]=591 to 595 n[b] (%)**	**Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1137 to 1147 n[b] (%)**	**Placebo Dose 2 N[a]=590 to 591 n[b] (%)**	**Pfizer-BioNTech COVID-19 Vaccine± Dose 3 N[a]=362 to 365 n[b] (%)**	**Placebo Dose 3 N[a]=170 n[b] (%)**
Redness[c]						
Any (≥0.5 cm)	124 (10.6)	44 (7.4)	107 (9.3)	39 (6.6)	26 (7.1)	9 (5.3)
Mild	114 (9.7)	41 (6.9)	97 (8.5)	36 (6.1)	17 (4.7)	8 (4.7)
Moderate	10 (0.9)	3 (0.5)	10 (0.9)	3 (0.5)	8 (2.2)	1 (0.6)
Severe	0	0	0	0	1 (0.3)	0

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1159 to 1173 n[b] (%)	Placebo Dose 1 N[a]=591 to 595 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1137 to 1147 n[b] (%)	Placebo Dose 2 N[a]=590 to 591 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 3 N[a]=362 to 365 n[b] (%)	Placebo Dose 3 N[a]=170 n[b] (%)
Swelling[c]						
Any (≥0.5 cm)	46 (3.9)	15 (2.5)	45 (3.9)	9 (1.5)	10 (2.7)	3 (1.8)
Mild	40 (3.4)	13 (2.2)	39 (3.4)	8 (1.4)	7 (1.9)	3 (1.8)
Moderate	6 (0.5)	2 (0.3)	6 (0.5)	1 (0.2)	3 (0.8)	0
Severe	0	0	0	0	0	0
Tenderness at the injection site[d]						
Any	192 (16.6)	66 (11.2)	171 (15.0)	50 (8.5)	58 (16.0)	20 (11.8)
Mild	181 (15.6)	61 (10.3)	154 (13.5)	42 (7.1)	51 (14.1)	17 (10.0)
Moderate	11 (0.9)	5 (0.8)	16 (1.4)	8 (1.4)	7 (1.9)	3 (1.8)
Severe	0	0	1 (0.1)	0	0	0

* Randomized participants who received at least 1 dose of the study intervention.
± Pfizer-BioNTech COVID-19 Vaccine (3 mcg modRNA).
Note: Reactions were collected in an electronic diary (e-diary) from Day 1 to Day 7 after vaccination.
a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: ≥0.5 to ≤2.0 cm; Moderate: >2.0 to ≤7.0 cm; Severe: >7.0 cm.
d. Mild: hurts if gently touched; Moderate: hurts if gently touched with crying; Severe: causes limitation of limb movement.

Table 12: Study 3 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 6 Through 23 Months of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 N[a]=1159 to 1173 n[b] (%)	Placebo Dose 1 N[a]=591 to 595 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 N[a]=1137 to 1147 n[b] (%)	Placebo Dose 2 N[a]=590 to 591 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 3 N[a]=362 to 365 n[b] (%)	Placebo Dose 3 N[a]=170 n[b] (%)
Fever						
≥38.0°C	85 (7.2)	43 (7.2)	85 (7.4)	36 (6.1)	25 (6.8)	10 (5.9)
≥38.0°C to 38.4°C	42 (3.6)	22 (3.7)	41 (3.6)	18 (3.0)	14 (3.8)	7 (4.1)
>38.4°C to 38.9°C	23 (2.0)	14 (2.4)	20 (1.7)	11 (1.9)	5 (1.4)	2 (1.2)
>38.9°C to 40.0°C	19 (1.6)	6 (1.0)	23 (2.0)	7 (1.2)	5 (1.4)	1 (0.6)
>40.0°C	1 (0.1)	1 (0.2)	1 (0.1)	0	1 (0.3)	0

	Pfizer-BioNTech COVID-19 Vaccine± Dose 1 Na=1159 to 1173 nb (%)	Placebo Dose 1 Na=591 to 595 nb (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 2 Na=1137 to 1147 nb (%)	Placebo Dose 2 Na=590 to 591 nb (%)	Pfizer-BioNTech COVID-19 Vaccine± Dose 3 Na=362 to 365 nb (%)	Placebo Dose 3 Na=170 nb (%)
Decreased appetite[c]						
Any	257 (22.2)	125 (21.2)	252 (22.2)	106 (18.0)	73 (20.2)	23 (13.5)
Mild	138 (11.9)	73 (12.4)	157 (13.8)	63 (10.7)	42 (11.6)	13 (7.6)
Moderate	116 (10.0)	51 (8.6)	91 (8.0)	42 (7.1)	27 (7.5)	10 (5.9)
Severe	3 (0.3)	1 (0.2)	4 (0.4)	1 (0.2)	4 (1.1)	0
Drowsiness[d]						
Any	313 (27.0)	173 (29.3)	271 (23.8)	125 (21.2)	72 (19.9)	22 (12.9)
Mild	251 (21.7)	130 (22.0)	201 (17.7)	98 (16.6)	50 (13.8)	15 (8.8)
Moderate	60 (5.2)	41 (6.9)	66 (5.8)	26 (4.4)	21 (5.8)	6 (3.5)
Severe	2 (0.2)	2 (0.3)	4 (0.4)	1 (0.2)	1 (0.3)	1 (0.6)
Irritability[e]						
Any	593 (51.2)	279 (47.2)	539 (47.4)	240 (40.7)	158 (43.6)	64 (37.6)
Mild	245 (21.1)	106 (17.9)	213 (18.7)	89 (15.1)	56 (15.5)	27 (15.9)
Moderate	341 (29.4)	173 (29.3)	319 (28.1)	146 (24.7)	101 (27.9)	37 (21.8)
Severe	7 (0.6)	0	7 (0.6)	5 (0.8)	1 (0.3)	0
Use of antipyretic or pain medication[f]	281 (24.0)	117 (19.7)	243 (21.2)	111 (18.8)	70 (19.2)	28 (16.5)

* Randomized participants who received at least 1 dose of the study intervention.
± Pfizer-BioNTech COVID-19 Vaccine (3 mcg modRNA).
Note: Events and use of antipyretic or pain medication were collected in an electronic diary (e-diary) from Day 1 to Day 7 after each dose.
a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: decreased interest in eating; Moderate: decreased oral intake; Severe: refusal to feed.
d. Mild: increased or prolonged sleeping bouts; Moderate: slightly subdued interfering with daily activity; Severe: disabling; not interested in usual daily activity.
e. Mild: easily consolable; Moderate: requiring increased attention; Severe: inconsolable; crying cannot be comforted.
f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

In the following analyses of Study 3 in participants 6 through 23 months of age (386 of whom received Pfizer-BioNTech COVID-19 Vaccine and 184 of whom received placebo), 83.7% of participants had at least 30 days of follow-up after Dose 3.

Serious Adverse Events
Serious adverse events from Dose 1 through 1 month after Dose 3, with an overall median of 1.3 months follow-up after Dose 3 were reported by 1.4% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 2.3% of placebo recipients. No serious adverse events were reported that were considered related to vaccination.

Non-Serious Adverse Events
Non-serious adverse events from Dose 1 through up to 1 month after Dose 3, in ongoing follow-up were reported by 29.1% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 26.3% of placebo recipients.

From Dose 1 through 30 days after Dose 3, lymphadenopathy was reported in 2 (0.2%) participants in the Pfizer-BioNTech COVID-19 Vaccine group vs. 0 (0%) in the placebo group. There were no other notable patterns between treatment groups for specific categories of non-serious adverse events that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Third Primary Series Dose in Individuals with Certain Kinds of Immunocompromise

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, in 99 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously 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 in recipients who were followed for 1 month following post Dose 3.

Pfizer-BioNTech COVID-19 Vaccine Administered as a First Booster Dose Following a Primary Series of Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY (COVID-19 Vaccine, mRNA) in Participants 18 through 55 Years of Age

A subset of Study 2 Phase 2/3 participants of 306 participants 18 through 55 years of age received a first booster dose of Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) approximately 6 months (range of 4.8 to 8.0 months) after completing the primary series. Additionally, a total of 23 Study 2 (Phase 1) participants (11 participants 18 through 55 years of age and 12 participants 65 through 85 years of age) received a first booster dose of Pfizer-BioNTech COVID-19 Vaccine approximately 8 months (range 7.9 to 8.8 months) after completing the primary series. Participants were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events through 1 month after vaccination and for serious adverse events for 6 months after the last vaccination.

Among the 306 Phase 2/3 participants, the median age was 42 years (range 19 through 55 years of age), 45.8% were male and 54.2% were female, 81.4% were White, 27.8% were Hispanic/Latino, 9.2% were Black or African American, 5.2% were Asian, and 0.7% were American Indian/Alaska Native. Among the 12 Phase 1 participants 65 through 85 years of age, the median age was 69 years (range 65 through 75 years of age), 6 were male and all were White and Not Hispanic/Latino. Following the booster dose, the median follow-up time was 2.6 months (range 2.1 to 2.9 months) for Phase 1 participants and 2.6 months (range 1.1 to 2.8 months) for Phase 2/3 participants.

Solicited Local and Systemic Adverse Reactions

Table 13 and Table 14 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of a first booster dose with Pfizer-BioNTech COVID-19 Vaccine for Phase 2/3 participants 18 through 55 years of age.

In participants who received a first booster dose, the mean duration of pain at the injection site was 2.6 days (range 1 to 8 days), for redness 2.2 days (range 1 to 15 days), and for swelling 2.2 days (range 1 to 8 days).

Table 13: Study 2 – Frequency and Percentages of Participants With Solicited Local Adverse Reactions, By Maximum Severity, Within 7 Days After a First Booster Dose of Pfizer-BioNTech COVID-19 Vaccine – Participants 18 through 55 Years of Age*

Solicited Local Adverse Reaction	Pfizer-BioNTech COVID-19 Vaccine± First Booster Dose N[a]=289 n[b] (%)
Redness[c]	
Any (>2 cm)	17 (5.9)
Mild	10 (3.5)
Moderate	7 (2.4)
Severe	0
Swelling[c]	
Any (>2 cm)	23 (8.0)
Mild	13 (4.5)
Moderate	9 (3.1)
Severe	1 (0.3)
Pain at the injection site[d]	
Any	240 (83.0)
Mild	174 (60.2)
Moderate	65 (22.5)
Severe	1 (0.3)

Note: Adverse Reactions were collected in the electronic diary (e-diary) from day of vaccination (Day 1) to Day 7 after the booster dose.

Note: No Grade 4 solicited local adverse reactions were reported.

* A subset of Phase 2/3 participants 18 through 55 years of age who received a booster dose of COMIRNATY (COVID-19 Vaccine, mRNA) approximately 6 months after completing the primary series.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.

b. n = Number of participants with the specified reaction.

c. Mild: >2.0 to 5.0 cm; Moderate: >5.0 to 10.0 cm; Severe: >10.0 cm.

d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

Table 14: Study 2 – Frequency and Percentages of Participants With Solicited Systemic Adverse Reactions, by Maximum Severity, Within 7 Days After a First Booster Dose with Pfizer-BioNTech COVID-19 Vaccine – Participants 18 through 55 Years of Age[*]

Solicited Systemic Adverse Reaction	Pfizer-BioNTech COVID-19 Vaccine[±] First Booster Dose N[a]=289 n[b] (%)
Fever	
≥38.0°C	25 (8.7)
≥38.0°C to 38.4°C	12 (4.2)
>38.4°C to 38.9°C	12 (4.2)
>38.9°C to 40.0°C	1 (0.3)
>40.0°C	0
Fatigue[c]	
Any	184 (63.7)
Mild	68 (23.5)
Moderate	103 (35.6)
Severe	13 (4.5)
Headache[c]	
Any	140 (48.4)
Mild	83 (28.7)
Moderate	54 (18.7)
Severe	3 (1.0)
Chills[c]	
Any	84 (29.1)
Mild	37 (12.8)
Moderate	44 (15.2)
Severe	3 (1.0)
Vomiting[d]	
Any	5 (1.7)
Mild	5 (1.7)
Moderate	0
Severe	0
Diarrhea[e]	
Any	25 (8.7)
Mild	21 (7.3)
Moderate	4 (1.4)
Severe	0
New or worsened muscle pain[c]	
Any	113 (39.1)
Mild	52 (18.0)
Moderate	57 (19.7)
Severe	4 (1.4)
New or worsened joint pain[c]	
Any	73 (25.3)
Mild	36 (12.5)
Moderate	36 (12.5)
Severe	1 (0.3)

Solicited Systemic Adverse Reaction	Pfizer-BioNTech COVID-19 Vaccine± First Booster Dose N[a]=289 n[b] (%)
Use of antipyretic or pain medication[f]	135 (46.7)

Note: Adverse reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from day of vaccination (Day 1) to Day 7 after the booster dose.
Note: No Grade 4 solicited systemic adverse reactions were reported.

* A subset of Phase 2/3 participants 18 through 55 years of age who received a booster dose of COMIRNATY (COVID-19 Vaccine, mRNA) approximately 6 months after completing the primary series.
a. N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. n = Number of participants with the specified reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.
± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

In Phase 1 participants ≥65 years of age (n=12), local reaction pain at the injection site (n=8, 66.7%) and systemic reactions fatigue (n=5, 41.7%), headache (n=5, 41.7%), chills (n=2, 16.7%), muscle pain (n=4, 33.3%), and joint pain (n=2, 16.7%) were reported after the booster dose. No participant in this age group reported a severe systemic event or fever after the booster dose.

Unsolicited Adverse Events

Overall, the 306 participants who received a first booster dose, had a median follow-up time of 2.6 months after the booster dose to the cutoff date (June 17, 2021).

In an analysis of all unsolicited adverse events reported following the first booster dose, through 1 month after the booster dose, in participants 18 through 55 years of age (N=306), those assessed as adverse reactions not already captured by solicited local and systemic reactions were lymphadenopathy (n=16, 5.2%), nausea (n=2, 0.7%), decreased appetite (n=1, 0.3%), rash (n=1, 0.3%), and pain in extremity (n=1, 0.3%).

Serious Adverse Events

Of the 306 participants who received a first booster dose of Pfizer-BioNTech COVID-19 Vaccine, there were no serious adverse events reported from the booster dose through 30 days after the booster dose. One participant reported a serious adverse event 61 days after the booster dose that was assessed as unrelated to vaccination.

First Booster Dose Following a Primary Series of Pfizer-BioNTech COVID-19 in Participants 5 Through 11 Years of Age

A subset of Phase 2/3 participants 5 through 11 years of age received a first booster dose of Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) at least 5 months after completing the primary series (range 5 to 9 months, 86.8% of participants received a booster dose at least 8 months after Dose 2). Those participants vaccinated prior to February 22, 2022 provided the safety database (n=401), and had a median safety follow-up of 1.3 months from vaccination through the data cutoff date of March 22, 2022.

The median age of these 401 participants was 8.0 years (range 5 through 11 years of age), 52.4% were male and 47.6% were female, 70.1% were White, 7.2% were Black or African American, 22.9% were Hispanic/Latino, 7.7% were Asian, and 2.0% were American Indian/Alaska Native.

Solicited Local and Systemic Adverse Reactions

Table 15 and Table 16 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of a booster dose of Pfizer-BioNTech COVID-19 Vaccine for Phase 2/3 participants 5 through 11 years of age.

In participants who received a booster dose, the mean duration of pain at the injection site after the booster dose was 2.4 days (range 1 to 35 days), for redness 2.3 days (range 1 to 12 days), and for swelling 2.3 days (range 1 to 9 days).

Table 15: Study 3 – Frequency and Percentages of Participants With Solicited Local Reactions, By Maximum Severity, Within 7 Days After the Booster Dose of Pfizer-BioNTech COVID-19 Vaccine – Participants 5 through 11 Years of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine± Booster N[a]=371 n[b] (%)
Redness[c]	
Any (≥0.5 cm)	58 (15.6)
Mild	38 (10.2)
Moderate	19 (5.1)
Severe	1 (0.3)
Swelling[c]	
Any (≥0.5 cm)	61 (16.4)
Mild	30 (8.1)
Moderate	31 (8.4)
Severe	0
Pain at the injection site[d]	
Any	274 (73.9)
Mild	177 (47.7)
Moderate	95 (25.6)
Severe	2 (0.5)

* Randomized participants who received at least 1 dose of the study intervention.

± Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA).

Note: Reactions were collected in the e-diary and unscheduled clinical assessments from Day 1 through Day 7 after vaccination.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. n = Number of participants with the specified characteristic.
c. Mild: ≥0.5 to 2.0 cm; moderate: >2.0 to 7.0 cm; severe: >7.0 cm.
d. Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity.

Table 16: Study 3 – Frequency and Percentages of Participants With Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After the Booster Dose of Pfizer-BioNTech COVID-19 Vaccine – Participants 5 through 11 Years of Age – Safety Population[*]

Solicited Systemic Reaction	Pfizer-BioNTech COVID-19 Vaccine[±] Booster N[a]=371 n[b] (%)
Fever	
≥38.0°C	25 (6.7)
≥38.0°C to 38.4°C	17 (4.6)
>38.4°C to 38.9°C	5 (1.3)
>38.9°C to 40.0°C	3 (0.8)
>40.0°C	0
Fatigue[c]	
Any	169 (45.6)
Mild	99 (26.7)
Moderate	63 (17.0)
Severe	7 (1.9)
Headache[c]	
Any	126 (34.0)
Mild	76 (20.5)
Moderate	47 (12.7)
Severe	0
Chills[c]	
Any	39 (10.5)
Mild	23 (6.2)
Moderate	15 (4.0)
Severe	1 (0.3)
Vomiting[d]	
Any	9 (2.4)
Mild	6 (1.6)
Moderate	3 (0.8)
Severe	0
Diarrhea[e]	
Any	18 (4.9)
Mild	15 (4.0)
Moderate	2 (0.5)
Severe	1 (0.3)
New or worsened muscle pain[c]	
Any	68 (18.3)
Mild	40 (10.8)
Moderate	28 (7.5)
Severe	0

Solicited Systemic Reaction	Pfizer-BioNTech COVID-19 Vaccine± Booster N[a]=371 n[b] (%)
New or worsened joint pain[c]	
Any	25 (6.7)
Mild	14 (3.8)
Moderate	11 (3.0)
Severe	0
Use of antipyretic or pain medication[f]	114 (30.7)

* Randomized participants who received at least 1 dose of the study intervention.
± Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA).
Note: Events and use of antipyretic or pain medication were collected in the e-diary and unscheduled clinical assessments from Day 1 through Day 7 after vaccination.
a. N = number of participants reporting at least 1 yes or no response for the specified event after the specified dose.
b. n = Number of participants with the specified characteristic.
c. Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity.
d. Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration.
e. Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Overall, the 401 participants who received a first booster dose of Pfizer-BioNTech COVID-19 Vaccine had a median follow-up time of 1.3 months after the booster dose through the cutoff date.

In an analysis of all unsolicited adverse events reported in participants 5 through 11 years of age (N=401) through up to 1 month after a first booster dose, lymphadenopathy (n=10, 2.5%) was an adverse reaction not already captured by solicited local and systemic reactions.

Serious Adverse Events

No serious adverse events were reported after the first booster dose through the cutoff date.

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

The safety of a Pfizer-BioNTech 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 Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) booster dose administered following completion of Pfizer-BioNTech COVID-19 Vaccine primary series (homologous booster dose) and from data from an independent National Institutes of Health (NIH) study Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States that evaluated a heterologous booster dose of the Pfizer-BioNTech COVID-19 Vaccine. In this study, participants 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 1 of 3 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 in the study following the Pfizer-BioNTech COVID-19 Vaccine heterologous booster dose did not identify any new safety concerns, as compared with adverse reactions reported following a Pfizer-BioNTech COVID-19 Vaccine primary series doses or homologous booster dose.

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

Safety surveillance data from the Ministry of Health of Israel on the administration of approximately 700,000 fourth doses of the Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) given at least 4 months after the third dose in participants 18 years of age and older (approximately 600,000 of whom were 60 years of age and older) revealed no new safety concerns.

Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

Study 5 (NCT05472038) enrolled participants 12 years of age and older to receive a booster (fourth dose) of Pfizer-BioNTech COVID-19 Vaccine, Bivalent (30 mcg modRNA). In Study 5, all participants 12 years of age and older are being monitored for safety throughout the study [through 6 months after the booster (fourth dose)].

Study 6 (NCT05543616) enrolled participants 6 months through 11 years of age to receive a booster (fourth dose) of Pfizer-BioNTech COVID-19 Vaccine, Bivalent.

In Study 6, all participants 6 months through 4 years of age were monitored for solicited local and systemic reactions and use of antipyretic medication after the vaccination in an electronic diary. Participants are being monitored for safety throughout the study [through 6 months after the booster (fourth dose)]. Tables 17 through 20 present the frequency and severity of solicited local and systemic reactions, within 7 days following a booster (fourth dose) of Pfizer-BioNTech COVID-19 Vaccine, Bivalent in participants 6 through 23 months of age and 2 through 4 years of age who were previously vaccinated with a 3-dose primary series of Pfizer-BioNTech COVID-19 Vaccine.

Participants 12 Years of Age and Older Who Received a Booster Dose with Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

A subset of Study 5 Phase 2/3 participants 12 through 17 years of age (n=107), 18 through 55 years of age (n=103) and 56 years of age and older (n=106) previously vaccinated with a 2-dose primary series and 1 booster dose of Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA), received a second booster dose with Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) (30 mcg modRNA).

The participants received the second booster dose a median of 9.9 months (range 5.5 to 14.3 months) after receiving the first booster dose and had a median follow-up time of 1.6 months up to a data cutoff date of October 12, 2022. The median age was 40.0 years, 53.2% were male, 46.8% were female, 81.3% were White, 9.2% were Hispanic/Latino, 5.1% were Asian, and 10.8% were Black or African American.

Unsolicited Adverse Events

In the following analysis of Study 5, 316 participants 12 years of age and older who received a second booster of Pfizer-BioNTech COVID-19 Vaccine, Bivalent had a median follow-up time of 1.6 months (range 1.3 to 1.8 months) to the cutoff date October 12, 2022.

Serious Adverse Events
Serious adverse events were reported in the 1 participant (considered unrelated to the vaccine) from the study vaccination through 1 month post vaccination.

Non-Serious Adverse Events
Lymphadenopathy 2 days post-vaccination, considered related to vaccination, was reported in 1 (0.3%) participant 12 years of age and older.

Participants 5 Through 11 Years of Age Who Received a Booster Dose with Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

In Study 6, 113 participants 5 through 11 years of age previously vaccinated with a 2-dose primary series and 1 booster dose of Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) received a booster (fourth dose) with Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) (10 mcg modRNA).

Participants received a booster (fourth dose) with Pfizer-BioNTech COVID-19, Bivalent 2.6 to 8.5 months after receiving their third dose with Pfizer-BioNTech COVID-19 Vaccine and had a median follow-up time of 1.6 months (range 1.1 to 2.3 months) up to a data cutoff date of November 25, 2022. Their median age was 9 years (range 5 through 11 years of age), 50.4% were male and 49.6% were female, 58.4% were White, 20.4% were Hispanic/Latino, 19.5% were multi-racial, 11.5% were Asian, and 8.0% were Black or African American.

Unsolicited Adverse Events

In the following analysis of Study 6, 113 participants 5 through 11 years of age who received a booster (fourth dose) with the Pfizer-BioNTech COVID-19 Vaccine, Bivalent had a median follow-up time of 1.6 months (range 1.1 to 2.3 months) to the cutoff date (November 25, 2022).

Serious Adverse Events
No serious adverse events were reported in the 113 participants 5 through 11 years of age from the study vaccination through 1 month post vaccination.

Non-Serious Adverse Events
Lymphadenopathy 2 days post-vaccination, considered related to vaccination, was reported in 1 (0.9%) participant 5 through 11 years of age.

Participants 2 Through 4 Years of Age Who Received a Booster Dose with Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

In a subset of Study 6, 36 participants 2 through 4 years of age previously vaccinated with a 3-dose primary series of Pfizer-BioNTech COVID-19 Vaccine (3 mcg modRNA) received a booster (fourth dose) with Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) (3 mcg modRNA).

Participants received a booster (fourth dose) with Pfizer-BioNTech COVID-19 Vaccine, Bivalent 2.2 to 8.5 months after receiving their third dose with Pfizer-BioNTech COVID-19 Vaccine and had a median follow-up time of 1.9 months (range 1.6 to 2.3 months) up to a data cutoff date of November 25, 2022. Their median age was 2 years (range 2 through 4 years of age), 55.6% were

male and 44.4% were female, 61.1% were White, 30.6% were Hispanic/Latino, 22.2% were multi-racial, 11.1% were Asian, and 5.6% were Black or African American.

Solicited Local and Systemic Adverse Reactions

Table 17 and Table 18 present the frequency and severity of reported solicited local reactions and systemic reactions, respectively, within 7 days of a booster (fourth dose) of Pfizer-BioNTech COVID-19 Vaccine, Bivalent.

The mean duration of pain at the injection site was 1.1 days (range 1 to 2 days), for redness 1.3 days (range 1 to 2 days), and for swelling 3 days for participants 2 through 4 years of age.

Table 17: Local Adverse Reactions, by Maximum Severity, Within 7 Days After a Booster (Fourth Dose) – Participants 2 through 4 Years of Age – Safety Population

	Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) 3 mcg modRNA N[a]=36 n[b] (%)
Redness[c]	
Any (≥0.5 cm)	3 (8.3)
Mild	2 (5.6)
Moderate	1 (2.8)
Swelling[c]	
Any (≥0.5 cm)	1 (2.8)
Mild	0
Moderate	1 (2.8)
Pain at the injection site[d]	
Any	10 (27.8)
Mild	8 (22.2)
Moderate	2 (5.6)

Note: Reactions were collected in the electronic diary (e-diary) and at unscheduled clinical assessments from Day 1 through Day 7 after the study vaccination. Reactions reported as adverse events in the case report form within 7 days after the study vaccination were also included in the analysis; the severity of these events is based on the grading scale in the adverse event section of the case report form.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
b. n = Number of participants with the specified characteristic.
c. Mild: ≥0.5 to 2.0 cm; Moderate: >2.0 to 7.0 cm; Severe: >7.0 cm. There were no reports of severe redness or swelling.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity. There were no reports of severe pain at injection site.

Table 18: Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After a Booster (Fourth Dose) – Participants 2 Through 4 Years of Age – Safety Population

	Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) 3 mcg modRNA N[a]=36 n[b] (%)
Fever	
≥38.0°C	0
Fatigue[c]	
Any	11 (30.6)
Mild	6 (16.7)
Moderate	5 (13.9)
Headache[c]	
Any	1 (2.8)
Mild	1 (2.8)
Chills[c]	
Any	1 (2.8)
Mild	1 (2.8)
Vomiting[d]	
Any	1 (2.8)
Mild	1 (2.8)
Diarrhea[e]	
Any	2 (5.6)
Mild	1 (2.8)
Moderate	1 (2.8)
New or worsened muscle pain[c]	
Any	0
New or worsened joint pain[c]	
Any	1 (2.8)
Mild	1 (2.8)
Use of antipyretic or pain medication[f]	1 (2.8)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) and at unscheduled clinical assessments from Day 1 through Day 7 after the study vaccination. Events reported as adverse events in the case report form within 7 days after the study vaccination were also included in the analysis; the severity of these events is based on the grading scale in the adverse event section of the case report form.

a. N = Number of participants reporting at least 1 yes or no response for the specified event after the study vaccination.
b. n = Number of participants with the specified characteristic.
c. Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity. There were no reports of severe fatigue or reports of moderate or severe headaches, chills, or new or worsened joint pain.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration. There were no reports of moderate or severe vomiting.
e. Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours. There were no reports of severe diarrhea.
f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Participants 2 through 4 years of age who received a booster (fourth dose) with the Pfizer-BioNTech COVID-19 Vaccine, Bivalent had a median follow-up time of 1.9 months (range 1.6 to 2.3 months) to the cutoff date (November 25, 2022).

Serious Adverse Events
No serious adverse events were reported in the 36 participants 2 through 4 years of age from the study vaccination through 1 month post vaccination.

Participants 6 Through 23 Months of Age Who Received a Booster Dose with Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5)

In a subset of Study 6, 24 participants 6 through 23 months previously vaccinated with a 3-dose primary series of Pfizer-BioNTech COVID-19 Vaccine (3 mcg modRNA) received a booster (fourth dose) of Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) (3 mcg modRNA).

Participants received a booster dose with Pfizer-BioNTech COVID-19 Vaccine, Bivalent 2.1 to 8.6 months after receiving their third dose with Pfizer-BioNTech COVID-19 and had a median follow-up time of 1.6 months (range 1.5 to 2.3 months) up to a data cutoff date of November 25, 2022. Their median age was 19 months (range 12 through 23 months), 58.3% were female and 41.7% were male, 54.2% were White, 20.8% were Asian, 20.8% were multi-racial, 16.7% were Hispanic/Latino, and 4.2% were Black or African American.

Solicited Local and Systemic Adverse Reactions

Table 19 and Table 20 present the frequency and severity of reported solicited local reactions and systemic reactions, respectively, within 7 days of a booster (fourth dose) of Pfizer-BioNTech COVID-19 Vaccine, Bivalent.

The duration of injection site tenderness, swelling and redness for all events observed was 1 day.

Table 19: Local Adverse Reactions, by Maximum Severity, Within 7 Days After a Booster (Fourth Dose) – Participants 6 Through 23 Months of Age – Safety Population

	Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) 3 mcg modRNA N[a]=24* n[b] (%)
Redness[c]	
Any (≥0.5 cm)	2 (8.3)
Mild	2 (8.3)
Swelling[c]	
Any (≥0.5 cm)	1 (4.2)
Mild	1 (4.2)
Tenderness at the injection site[d]	
Any	1 (4.3)
Mild	1 (4.3)

Note: Reactions were collected in the electronic diary (e-diary) and at unscheduled clinical assessments from Day 1 through Day 7 after the study vaccination. Reactions reported as adverse events in the case report form within 7 days after the study vaccination were also included in the analysis; the severity of these events is based on the grading scale in the adverse event section of the case report form.

* N = 23 for tenderness at the injection site.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.

b. n = Number of participants with the specified characteristic.

c. Mild: ≥0.5 to 2.0 cm; Moderate: >2.0 to 7.0 cm; Severe: >7.0 cm. There were no reports of moderate or severe redness or swelling.

d. Mild: hurts if gently touched; Moderate: hurts if gently touched with crying; Severe: causes limitation of limb movement. There were no reports of moderate or severe tenderness at the injection site.

Table 20: Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After a Booster (Fourth Dose) – Participants 6 Through 23 Months of Age – Safety Population

	Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) 3 mcg modRNA N[a]=24* n[b] (%)
Fever[c]	
≥38.0°C	1 (4.2)
≥38.0°C to 38.4°C	1 (4.2)
Decreased appetite[d]	
Any	1 (4.5)
Mild	1 (4.5)
Drowsiness[e]	
Any	2 (9.1)
Mild	2 (9.1)
Irritability[f]	
Any	4 (18.2)
Mild	3 (13.6)
Moderate	1 (4.5)
Use of antipyretic or pain medication[g]	2 (8.3)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) and at unscheduled clinical assessments from Day 1 through Day 7 after the study vaccination. Events reported as adverse events in the case report form within 7 days after the study vaccination were also included in the analysis; the severity of these events is based on the grading scale in the adverse event section of the case report form.

* N = 22 for decreased appetite, drowsiness, and irritability.

a. N = Number of participants reporting at least 1 yes or no response for the specified event after the study vaccination.

b. n = Number of participants with the specified characteristic.

c. There were no reports of fever >38.4°C.

d. Mild: decreased interest in eating; Moderate: decreased oral intake; Severe: refusal to feed. There were no reports of moderate or severe decreased appetite.

e. Mild: increased or prolonged sleeping bouts; Moderate: slightly subdued interfering with daily activity; Severe: disabling; not interested in usual daily activity. There were no reports of moderate or severe drowsiness.

f. Mild: easily consolable; Moderate: requiring increased attention; Severe: inconsolable; crying cannot be comforted. There were no reports of severe irritability.

g. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Participants 6 through 23 months of age who received a booster (fourth dose) with the Pfizer-BioNTech COVID-19 Vaccine, Bivalent had a median follow-up time of 1.6 months (range 1.5 to 2.3 months) to the cutoff date (November 25, 2022). In an analysis of all unsolicited adverse events reported following the booster dose through 1 month after the booster dose, the adverse reaction not already captured by solicited local and systemic reactions was injection site pain (n=1; 4.2%).

Serious Adverse Events
No serious adverse events were reported in the 24 participants 6 through 23 months of age from the study vaccination through 1 month post vaccination.

Non-Serious Adverse Events
Non-serious adverse events in participants 6 through 23 months of age from the study vaccination through 1 month post vaccination were reported in 3 (12.5%) Pfizer-BioNTech COVID-19 Vaccine, Bivalent recipients. Non-serious adverse events considered related to vaccination by the study investigator were fatigue (n=1; 4.2%) and injection site pain (n=1; 4.2%).

Bivalent Vaccine (Original and Omicron BA.1)

Bivalent Vaccine (Original and Omicron BA.1) Administered as a Second Booster Dose

In Study 4, a total of 610 participants greater than 55 years of age previously vaccinated with a 2-dose primary series and 1 booster dose of Pfizer-BioNTech COVID-19 Vaccine went on to receive a second booster dose with either Pfizer-BioNTech COVID-19 Vaccine or the bivalent vaccine (Original and Omicron BA.1).

The 305 participants greater than 55 years who received a second booster dose with Pfizer-BioNTech COVID-19 received it 5.3 to 13.1 months after receiving the first booster dose and had a median follow-up time of 1.8 months up to a data cutoff date of May 16, 2022. Their median age was 66 years (range 56 through 87 years of age), 47.5% were male and 52.5% were female, 87.9% were White, 18.7% were Hispanic/Latino, 4.3% were Asian, and 6.2% were Black or African American.

The 305 participants greater than 55 years who received a second booster dose with the bivalent vaccine (Original and Omicron BA.1) received it 4.7 to 11.5 months after receiving the first booster dose and had a median follow up time of 1.7 months up to a data cutoff date of May 16, 2022. Their median age was 67 years (range 56 through 85 years of age), 53.1% were male and 46.9% were female, 89.8% were White, 14.8% were Hispanic/Latino, 5.2% were Asian, and 4.3% were Black or African American.

Solicited Local and Systemic 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 Pfizer-BioNTech COVID-19 Vaccine. Events that persisted for more than 7 days were followed until resolution.

Table 21 and Table 22 present the frequency and severity of reported solicited local and systemic adverse reactions within 7 days following a second booster dose with Pfizer-BioNTech, Bivalent vaccine (Original and Omicron BA.1) booster dose compared to Pfizer-BioNTech COVID-19 Vaccine in participants greater than 55 years of age.

In participants who received the bivalent vaccine (Original and Omicron BA.1), the mean duration of injection site pain, redness, and swelling was 2.2 days (range 1 to 12 days), 2.9 days (range 1 to 10 days), and 1.9 days (range 1 to 4 days), respectively.

Table 21: Local Adverse Reactions, by Maximum Severity, Within 7 Days After a Second Booster Dose – Participants Greater Than 55 Years of Age – Safety Population

	Pfizer-BioNTech COVID-19 Vaccine N[a]=298 n[b] (%)	**Bivalent Vaccine (Original and Omicron BA.1) N[a]=301 n[b] (%)**
Redness[c]		
Any (>2 cm)	19 (6.4)	21 (7.0)
Mild	12 (4.0)	13 (4.3)
Moderate	6 (2.0)	8 (2.7)
Severe	1 (0.3)	0
Swelling[c]		
Any (>2 cm)	18 (6.0)	20 (6.6)
Mild	10 (3.4)	14 (4.7)
Moderate	8 (2.7)	6 (2.0)
Severe	0	0
Pain at the injection site[d]		
Any	179 (60.1)	175 (58.1)
Mild	154 (51.7)	159 (52.8)
Moderate	24 (8.1)	15 (5.0)
Severe	1 (0.3)	1 (0.3)

Note: Adverse Reactions were collected in the electronic diary (e-diary) from day of vaccination (Day 1) through Day 7 after the study vaccination.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the study vaccination.
b. n = Number of participants with the specified adverse reaction.
c. Mild: >2.0 to 5.0 cm; Moderate: >5.0 to 10.0 cm; Severe: >10.0 cm.
d. Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 22: Systemic Adverse Reactions, by Maximum Severity, Within 7 Days After the Second Booster Dose – Participants Greater Than 55 Years of Age – Safety Population

	Pfizer-BioNTech COVID-19 Vaccine N[a]=298 n[b] (%)	**Bivalent Vaccine (Original and Omicron BA.1) N[a]=301 n[b] (%)**
Fever		
≥38.0°C	11 (3.7)	15 (5.0)
≥38.0°C to 38.4°C	6 (2.0)	11 (3.7)
>38.4°C to 38.9°C	5 (1.7)	0
>38.9°C to 40.0°C	0	4 (1.3)
>40.0°C	0	0

	Pfizer-BioNTech COVID-19 Vaccine N[a]=298 n[b] (%)	Bivalent Vaccine (Original and Omicron BA.1) N[a]=301 n[b] (%)
Fatigue[c]		
Any	135 (45.3)	148 (49.2)
Mild	70 (23.5)	88 (29.2)
Moderate	64 (21.5)	55 (18.3)
Severe	1 (0.3)	5 (1.7)
Headache[c]		
Any	79 (26.5)	101 (33.6)
Mild	47 (15.8)	71 (23.6)
Moderate	31 (10.4)	29 (9.6)
Severe	1 (0.3)	1 (0.3)
Chills[c]		
Any	49 (16.4)	39 (13.0)
Mild	32 (10.7)	25 (8.3)
Moderate	17 (5.7)	14 (4.7)
Severe	0	0
Vomiting[d]		
Any	4 (1.3)	5 (1.7)
Mild	2 (0.7)	5 (1.7)
Moderate	2 (0.7)	0
Severe	0	0
Diarrhea[e]		
Any	13 (4.4)	27 (9.0)
Mild	10 (3.4)	18 (6.0)
Moderate	3 (1.0)	5 (1.7)
Severe	0	4 (1.3)
New or worsened muscle pain[c]		
Any	59 (19.8)	67 (22.3)
Mild	35 (11.7)	40 (13.3)
Moderate	24 (8.1)	27 (9.0)
Severe	0	0
New or worsened joint pain[c]		
Any	27 (9.1)	34 (11.3)
Mild	16 (5.4)	23 (7.6)
Moderate	11 (3.7)	11 (3.7)
Severe	0	0
Use of antipyretic or pain medication[f]	80 (26.8)	88 (29.2)

	Pfizer-BioNTech COVID-19 Vaccine N[a]=298 n[b] (%)	Bivalent Vaccine (Original and Omicron BA.1) N[a]=301 n[b] (%)

Note: Adverse reactions and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from day of vaccination (Day 1) through Day 7 after the study vaccination.

a. N = Number of participants reporting at least 1 yes or no response for the specified adverse reaction after the study vaccination.
b. n = Number of participants with the specified adverse reaction.
c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.
d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.
e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.
f. Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

Overall, the participants who received a second booster dose with the bivalent vaccine (Original and Omicron BA.1) had a median follow-up time of 1.7 months (range 1.0 to 2.0 months) to the cutoff date (May 16, 2022).

In an analysis of all unsolicited adverse events reported following the second booster dose, through 1 month after the booster dose, those assessed as adverse reactions not already captured by solicited local and systemic reactions were lymphadenopathy (n=1, 0.3%) for the Pfizer-BioNTech COVID-19 Vaccine and (n=1, 0.3%) for the bivalent vaccine (Original and Omicron BA.1), nausea (n=1, 0.3%) for the Pfizer-BioNTech COVID-19 Vaccine and (n=1, 0.3%) for the bivalent vaccine (Original and Omicron BA.1), and malaise (n=0) for the Pfizer-BioNTech COVID-19 Vaccine and (n=1, 0.3%) for the bivalent vaccine (Original and Omicron BA.1).

Serious Adverse Events
Serious adverse events up to 1 month after the second booster dose in ongoing follow up were reported by no Pfizer-BioNTech COVID-19 Vaccine recipients and by 1 bivalent vaccine (Original and Omicron BA.1) recipient (1 serious adverse event considered unrelated to the vaccine).

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-authorization use of Pfizer-BioNTech COVID-19 Vaccine and Pfizer-BioNTech 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
Gastrointestinal Disorders: diarrhea, vomiting
Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)
Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)
Nervous System Disorders: syncope, dizziness

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 Pfizer-BioNTech 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.

Instructions for Reporting to VAERS

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 Pfizer-BioNTech 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 Pfizer-BioNTech 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 “Pfizer-BioNTech 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 Pfizer Inc. using the contact information below or by providing a copy of the VAERS form to Pfizer Inc.

Website	Fax number	Telephone number
www.pfizersafetyreporting.com	1-866-635-8337	1-800-438-1985

7 DRUG INTERACTIONS

There are no data to assess the concomitant administration of Pfizer-BioNTech COVID-19 Vaccine, Bivalent with other vaccines.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

No data are available regarding the use of Pfizer-BioNTech COVID-19 Vaccine, Bivalent during pregnancy.

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 Pfizer-BioNTech COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

In a reproductive and developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (modRNA) (30 mcg) and other ingredients included in a single human dose of Pfizer-BioNTech COVID-19 Vaccine was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. 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 Pfizer-BioNTech COVID-19 Vaccine or the Pfizer-BioNTech COVID-19 Vaccine, Bivalent on the breastfed infant or on milk production/excretion.

8.4 Pediatric Use

Pfizer-BioNTech 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 Pfizer-BioNTech COVID-19 Vaccine, Pfizer-BioNTech COVID-19 Vaccine, Bivalent, and the bivalent vaccine (Original and Omicron BA.1).

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

8.5 Geriatric Use

Clinical studies of Pfizer-BioNTech COVID-19 Vaccine include participants 65 years of age and older who received the primary series and their data contributes to the overall assessment of safety and effectiveness of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent *[see Adverse Reactions (6.1), Clinical Studies (14)]*. Of the total number of Pfizer-BioNTech COVID-19 Vaccine recipients in Study 2 (N=20,033), 21.4% (n=4,294) were 65 years of age and older and 4.3% (n=860) were 75 years of age and older.

A clinical study with the bivalent vaccine (Original and Omicron BA.1) included 197 individuals 65 years of age and older and their data contribute to the overall assessment of safety and effectiveness of Pfizer-BioNTech COVID-19 Vaccine, Bivalent *[see Adverse Reactions (6.1), Clinical Studies (14)]*.

8.6 Use in Immunocompromised Individuals

From an independent report (*Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med*), safety and effectiveness of a third dose of the Pfizer-BioNTech COVID-19 vaccine have been evaluated in persons that received solid organ transplants. The administration of a third dose of vaccine appears to be only moderately effective in increasing potentially protective antibody titers. Patients should still be counselled 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

The Pfizer-BioNTech COVID-19 Vaccine, Bivalent does not contain preservative. The vial stoppers are not made with natural rubber latex.

Multiple Dose Vials with Maroon Caps and Labels with Maroon Borders

The Pfizer-BioNTech COVID-19 Vaccine, Bivalent in multiple dose vials with maroon caps and labels with maroon borders is supplied as a frozen suspension; each vial must be diluted with 2.2 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine.

Each 0.2 mL dose of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent supplied in multiple dose vials with maroon caps and labels with maroon borders is formulated to contain 1.5 mcg of modRNA encoding the S-glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original) and 1.5 mcg of modRNA encoding the S-glycoprotein of SARS-CoV-2 Omicron variant lineages BA.4 and BA.5 (Omicron BA.4/BA.5). The S-glycoproteins of the SARS-CoV-2 Omicron variant lineages BA.4 and BA.5 are identical. Each dose contains 3 mcg modRNA.

Each 0.2 mL dose of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent supplied in multiple dose vials with maroon caps and labels with maroon borders also includes the following ingredients: lipids (0.04 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.005 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.01 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.02 mg cholesterol), 3.2 mg sucrose, 0.006 mg tromethamine, and 0.04 mg tromethamine hydrochloride. The diluent (sterile 0.9% Sodium Chloride Injection, USP) contributes 1.52 mg sodium chloride per dose.

Multiple Dose Vials with Orange Caps and Labels with Orange Borders

The Pfizer-BioNTech COVID-19 Vaccine, Bivalent in multiple dose vials with orange caps and labels with orange borders is supplied as a frozen suspension; each vial must be diluted with 1.3 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine.

Each 0.2 mL dose of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent supplied in multiple dose vials with orange caps and labels with orange borders is formulated to contain 5 mcg of a nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original) and 5 mcg of modRNA encoding the S-glycoprotein of 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 contains 10 mcg modRNA.

Each 0.2 mL dose of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent supplied in multiple dose vials with orange caps and labels with orange borders also includes the following ingredients: lipids (0.14 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.02 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.03 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.06 mg cholesterol), 10.3 mg sucrose, 0.02 mg tromethamine, and 0.13 mg tromethamine hydrochloride. The diluent (sterile 0.9% Sodium Chloride Injection, USP) contributes 0.9 mg sodium chloride per dose.

Multiple Dose Vials and Single Dose Vials with Gray Caps and Labels with Gray Borders

The Pfizer-BioNTech COVID-19 Vaccine, Bivalent in multiple dose vials and single dose vials with gray caps and labels with gray borders is supplied as a sterile, frozen suspension. This presentation does not need to be diluted.

Each 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent supplied in multiple dose vials and single dose vials with gray caps and labels with gray borders is formulated to contain 15 mcg of a nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2 Wuhan-Hu-1 strain (Original) and 15 mcg of modRNA encoding the S glycoprotein of 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 contains 30 mcg modRNA.

Each 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent supplied in multiple dose and single dose vials with gray caps and labels with gray borders also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.19 mg cholesterol), 0.06 mg tromethamine, 0.4 mg tromethamine hydrochloride, and 31 mg sucrose.

12 CLINICAL PHARMACOLOGY

The modRNA in the Pfizer-BioNTech COVID-19 Vaccine, Bivalent is formulated in lipid particles, which enable delivery of the RNA 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 Pfizer-BioNTech COVID-19 Vaccine, Bivalent for individuals 6 months of age and older is based on:

- effectiveness of Pfizer-BioNTech COVID-19 Vaccine in individuals 6 months of age and older,
- immunogenicity of the bivalent vaccine (Original and Omicron BA.1) in individuals greater than 55 years of age, and
- immunogenicity of Pfizer-BioNTech COVID-19 Vaccine, Bivalent in individuals 6 months through 4 years of age.

14.1 Efficacy of 2-Dose Primary Series of Pfizer-BioNTech COVID-19 Vaccine in Participants 16 Years of Age and Older

Study 2 is a multicenter, multinational, Phase 1/2/3, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV).

In the Phase 2/3 portion of Study 2, based on data accrued through November 14, 2020, approximately 44,000 participants 12 years of age and older were randomized equally and received 2 doses of Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) or placebo separated by 21 days. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The population for the analysis of the primary efficacy endpoint included 36,621 participants 12 years of age and older (18,242 in the Pfizer-BioNTech COVID-19 Vaccine group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. Table 23 presents the specific demographic characteristics in the studied population.

Table 23: Demographics (population for the primary efficacy endpoint)[a]

	Pfizer-BioNTech COVID-19 Vaccine* (N=18,242) n (%)	**Placebo (N=18,379) n (%)**
Sex		
Male	9318 (51.1)	9225 (50.2)
Female	8924 (48.9)	9154 (49.8)
Age (years)		
Mean (SD)	50.6 (15.70)	50.4 (15.81)
Median	52.0	52.0
Min, max	(12, 89)	(12, 91)
Age group		
≥12 through 15 years[b]	46 (0.3)	42 (0.2)
≥16 through 17 years	66 (0.4)	68 (0.4)
≥16 through 64 years	14,216 (77.9)	14,299 (77.8)
≥65 through 74 years	3176 (17.4)	3226 (17.6)
≥75 years	804 (4.4)	812 (4.4)
Race		
White	15,110 (82.8)	15,301 (83.3)
Black or African American	1617 (8.9)	1617 (8.8)
American Indian or Alaska Native	118 (0.6)	106 (0.6)
Asian	815 (4.5)	810 (4.4)
Native Hawaiian or other Pacific Islander	48 (0.3)	29 (0.2)
Other[c]	534 (2.9)	516 (2.8)
Ethnicity		
Hispanic or Latino	4886 (26.8)	4857 (26.4)
Not Hispanic or Latino	13,253 (72.7)	13,412 (73.0)
Not reported	103 (0.6)	110 (0.6)
Comorbidities[d]		
Yes	8432 (46.2)	8450 (46.0)
No	9810 (53.8)	9929 (54.0)

* Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

a. All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window, have no other important protocol deviations as determined by the clinician, and have no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2.

b. 100 participants 12 through 15 years of age with limited follow-up in the randomized population received at least 1 dose (49 in the vaccine group and 51 in the placebo group). Some of these participants were included in the

efficacy evaluation depending on the population analyzed. They contributed to exposure information but with no confirmed COVID-19 cases, and did not affect efficacy conclusions.

c. Includes multi-racial and not reported.

d. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease
   - Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma
   - Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension)
   - Obesity (body mass index ≥30 kg/m^2)
   - Diabetes (Type 1, Type 2 or gestational)
   - Liver disease
   - Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)

The population in the primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

The vaccine efficacy information is presented in Table 24.

Table 24: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**Pfizer-BioNTech COVID-19 Vaccine± Na=18,198 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=18,325 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CI)**
All subjects[e]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[f]
16 through 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[g]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[g]

First COVID-19 occurrence from 7 days after Dose 2 in participants with or without evidence of prior SARS-CoV-2 infection			
Subgroup	**Pfizer-BioNTech COVID-19 Vaccine± Na=19,965 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=20,172 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CI)**
All subjects[e]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[f]
16 through 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[g]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[g]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. No confirmed cases were identified in participants 12 through 15 years of age.

f. Credible interval for vaccine efficacy (VE) was calculated using a beta-binomial model with a beta (0.700102, 1) prior for $\theta=r(1-VE)/(1+r(1-VE))$, where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.

g. Confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

14.2 Efficacy of 2-Dose Primary Series of Pfizer-BioNTech COVID-19 Vaccine in Participants 12 Through 15 Years of Age

A descriptive efficacy analysis of Study 2 has been performed in approximately 2,200 participants 12 through 15 years of age evaluating confirmed COVID-19 cases accrued up to a data cutoff date of March 13, 2021.

The efficacy information in participants 12 through 15 years of age is presented in Table 25.

Table 25: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2: Without Evidence of Infection and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period, Participants 12 Through 15 Years of Age Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants 12 through 15 years of age without evidence of prior SARS-CoV-2 infection*			
	Pfizer-BioNTech COVID-19 Vaccine± N[a]=1005 Cases n1[b] Surveillance Time[c] (n2[d])	**Placebo N[a]=978 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
Participants 12 through 15 years of age	0 0.154 (1001)	16 0.147 (972)	100.0 (75.3, 100.0)
First COVID-19 occurrence from 7 days after Dose 2 in participants 12 through 15 years of age with or without evidence of prior SARS-CoV-2 infection			
	Pfizer-BioNTech COVID-19 Vaccine± N[a]=1119 Cases n1[b] Surveillance Time[c] (n2[d])	**Placebo N[a]=1110 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI[e])**
Participants 12 through 15 years of age	0 0.170 (1109)	18 0.163 (1094)	100.0 (78.1, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

e. Confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

14.3 Efficacy of 2-Dose Primary Series of Pfizer-BioNTech COVID-19 Vaccine in Participants 5 Through 11 Years of Age

A descriptive efficacy analysis of Study 3 has been performed in 1,968 participants 5 through 11 years of age without evidence of infection prior to 7 days after Dose 2. This analysis evaluated confirmed symptomatic COVID-19 cases accrued up to a data cutoff date of October 8, 2021.

Table 26 presents the specific demographic characteristics in participants who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose.

Table 26: Demographics Characteristics – Participants Without Evidence of Infection Prior to 7 Days After Dose 2 – Phase 2/3 – 5 Through 11 Years of Age – Evaluable Efficacy Population

	Pfizer-BioNTech COVID-19 Vaccine* 10 mcg/Dose (N^a=1305) n^b (%)	**Placebo (N^a=663) n^b (%)**
Sex		
Male	679 (52.0)	343 (51.7)
Female	626 (48.0)	320 (48.3)
Age at Vaccination		
Mean (SD)	8.2 (1.93)	8.1 (1.98)
Median	8.0	8.0
Min, max	(5, 11)	(5, 11)
Race		
White	1018 (78.0)	514 (77.5)
Black or African American	76 (5.8)	48 (7.2)
American Indian or Alaska Native	<1.0%	<1.0%
Asian	86 (6.6)	46 (6.9)
Native Hawaiian or other Pacific Islander	<1.0%	<1.0%
Other[c]	110 (8.4)	52 (7.8)
Ethnicity		
Hispanic or Latino	243 (18.6)	130 (19.6)
Not Hispanic or Latino	1059 (81.1)	533 (80.4)
Not reported	<1.0%	<1.0%
Comorbidities[d]		
Yes	262 (20.1)	133 (20.1)
No	1043 (79.9)	530 (79.9)

* Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA).

a. N = number of participants in the specified group from the evaluable efficacy population with no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2. This value is the denominator for the percentage calculations. Evaluable efficacy population included all eligible randomized participants who received all vaccination(s) as randomized within the predefined window, had no other important protocol deviations as determined by the clinician.

b. n = Number of participants with the specified characteristic.

c. Includes multiracial and not reported.

d. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as participants who had at least 1 of the prespecified comorbidities based on MMWR 69(32);1081-1088 and/or obesity (BMI ≥ 95th percentile).

The descriptive vaccine efficacy results in participants 5 through 11 years of age without evidence of prior SARS-CoV-2 infection are presented in Table 27. None of the cases accrued met criteria for severe COVID-19 or multisystem inflammatory syndrome in children (MIS-C). No cases of COVID-19 were observed in either the vaccine group or the placebo group in participants with evidence of prior SARS-CoV-2 infection.

Table 27: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2: Without Evidence of Infection Prior to 7 Days After Dose 2 – Phase 2/3 – Participants 5 Through 11 Years of Age Evaluable Efficacy Population

First COVID-19 occurrence from 7 days after Dose 2 in participants 5 through 11 years of age without evidence of prior SARS-CoV-2 infection*			
	Pfizer-BioNTech COVID-19 Vaccine± 10 mcg/dose N[a]=1305 Cases n1[b] Surveillance Time[c] (n2[d])	**Placebo N[a]=663 Cases n1[b] Surveillance Time[c] (n2[d])**	**Vaccine Efficacy % (95% CI)**
Participants 5 through 11 years of age	3 0.322 (1273)	16 0.159 (637)	90.7 (67.7, 98.3)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

± Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA).

a. N = Number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.

14.4 Immunogenicity of 2-Dose Primary Series of Pfizer-BioNTech COVID-19 Vaccine in Participants 5 Through 11 Years of Age

SARS-CoV-2 50% neutralizing antibody titers (NT50) 1 month after the primary series were compared between randomly selected subsets of Phase 2/3 participants 5 through 11 years of age from study C4591007 and the efficacy study C4591001 Phase 2/3 participants 16 through 25 years of age, using a microneutralization assay against the reference strain (USA_WA1/2020). The primary immunobridging analyses compared the geometric mean titers (using a geometric mean ratio [GMR]) and the seroresponse (defined as achieving at least 4-fold rise in SARS-CoV-2 NT50 from before Dose 1) rates in the evaluable immunogenicity population of participants without evidence of prior SARS-CoV-2 infection up to 1 month after Dose 2 in each group. The prespecified immunobridging criteria were met for both the GMR and the seroresponse difference (Table 28 and Table 29).

Table 28: SARS-CoV-2 GMTs (NT50) at 1 Month After Primary Series – Immunobridging Subset - Participants 5 Through 11 Years of Age (Study 3) and Participants 16 Through 25 Years of Age (Study 2) – Without Evidence of SARS-CoV-2 Infection up to 1 Month After Dose 2 – Evaluable Immunogenicity Population

		Pfizer-BioNTech COVID-19 Vaccine		GMT Ratio (95%CI) (5 Through 11 Years of Age/ 16 Through 25 Years of Age)[d,e]
		10 mcg/Dose* 5 Through 11 Years of Age n[a]=264	30 mcg/Dose± 16 Through 25 Years of Age n[a]=253	
Assay	Time Point[b]	GMT[c] (95% CI[c])	GMT[c] (95% CI[c])	
SARS-CoV-2 neutralization assay - NT50 (titer)[f]	1 month after Dose 2	1197.6 (1106.1, 1296.6)	1146.5 (1045.5, 1257.2)	1.04 (0.93, 1.18)

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMT = geometric mean titer; LLOQ = lower limit of quantitation; NAAT = nucleic acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Participants who had no serological or virological evidence (up to 1 month post-Dose 2 blood sample collection) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at pre-Dose 1 and 1 month after Dose 2, SARS-CoV-2 not detected by NAAT [nasal swab] at pre-Dose 1 and pre-Dose 2, and negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2 blood collection) and had no medical history of COVID-19 were included in the analysis.

* Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA).

± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

a. n = Number of participants with valid and determinate assay results for the specified assay at the given dose/sampling time point.

b. Protocol-specified timing for blood sample collection.

c. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

d. GMT ratio and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titers (5 through 11 years of age minus 16 through 25 years of age) and the corresponding CI (based on the Student t distribution).

e. Immunobridging is declared if the lower bound of the 2-sided 95% CI for the GMT ratio is greater than 0.67 and the point estimate of the GMR is ≥0.8.

f. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

Table 29: Difference in Percentages of Participants with Seroresponse at 1 Month After Primary Series – Immunobridging Subset – Participants 5 Through 11 Years of Age (Study 3) and Participants 16 Through 25 Years of Age (Study 2) Without Evidence of Infection up to 1 Month After Dose 2 – Evaluable Immunogenicity Population

		Pfizer-BioNTech COVID-19 Vaccine		Difference in Seroresponse Rates %[e] (95% CI[f]) (5 Through 11 Years of Age minus 16 Through 25 Years of Age)[g]
		10 mcg/Dose* 5 Through 11 Years of Age N[a]=264	30 mcg/Dose± 16 Through 25 Years of Age N[a]=253	
Assay	Time Point[b]	n[c] (%) (95% CI[d])	n[c] (%) (95% CI[d])	
SARS-CoV-2 neutralization assay - NT50 (titer)[h]	1 month after Dose 2	262 (99.2) (97.3, 99.9)	251 (99.2) (97.2, 99.9)	0.0 (-2.0, 2.2)

Abbreviations: LLOQ = lower limit of quantitation; NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein–binding; NT50 = 50% neutralizing titer 50; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Seroresponse is defined as achieving a ≥4-fold rise from baseline (before Dose 1). If the baseline measurement is below the LLOQ, a postvaccination assay result ≥4 × LLOQ is considered a seroresponse

Note: Participants who had no serological or virological evidence (up to 1 month post-Dose 2 blood sample collection) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at pre-Dose 1 and 1 month after Dose 2, SARS-CoV-2 not detected by NAAT [nasal swab] at pre-Dose 1 and pre-Dose 2, and negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2 blood collection) and had no medical history of COVID-19 were included in the analysis.

* Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA).

± Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

a. N = number of participants with valid and determinate assay results both before vaccination and at 1 month after Dose 2. These values are the denominators for the percentage calculations.

b. Protocol-specified timing for blood sample collection.

c. n = Number of participants with seroresponse for the given assay at the given dose/sampling time point.

d. Exact 2-sided CI based on the Clopper and Pearson method.

e. Difference in proportions, expressed as a percentage (5 through 11 years of age minus 16 through 25 years of age).

f. 2-Sided CI, based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

g. Immunobridging is declared if the lower bound of the 2-sided 95% CI for the difference in proportions is greater than -10.0% provided that the immunobridging criteria based on GMR were met.

h. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

14.5 Efficacy of 3-Dose Primary Series of Pfizer-BioNTech COVID-19 Vaccine in Participants 6 Months Through 4 Years of Age

Study 3 is an ongoing Phase 1/2/3 multicenter, randomized, dose finding, open label (Phase 1) and multinational, saline placebo-controlled, observer-blind, immunogenicity and efficacy (Phase 2/3) study to evaluate the safety and effectiveness of Pfizer-BioNTech COVID-19 Vaccine in individuals 6 months through 11 years of age. Randomization was stratified by age: 6 through 23 months of age, 2 through 4 years of age, or 5 through 11 years of age. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Results from participants 6 months through 4 years of age are presented in this subsection. In

Phase 2/3, a total of 1,776 participants 6 through 23 months of age and 2,750 participants 2 through 4 years of age were randomized 2:1 and received 3 doses of the Pfizer-BioNTech COVID-19 Vaccine or saline placebo.

Effectiveness in individuals 6 months through 4 years of age is based on a comparison of immune responses in this age group to individuals 16 through 25 years of age.

Immunogenicity in Participants 2 Through 4 Years of Age After a 3-Dose Primary Series

Immunogenicity analyses have been performed in the immunobridging subset of 143 Study 3 participants 2 through 4 years of age without evidence of infection up to 1 month after Dose 3 based on a data cutoff date of April 29, 2022.

The evaluable immunogenicity population without prior evidence of SARS-CoV-2 infection up to 1 month after Dose 3 of Pfizer-BioNTech COVID-19 Vaccine was comprised of 143 participants 2 through 4 years of age. Most participants in this analysis population were White (69.2%), with 5.6% Black or African American participants, 11.2% Asian participants, and 11.9% multiracial participants. There were 11.2% Hispanic/Latino participants. The median age was 3.0 years and 44.1% of participants were male. There were 6.3% of participants reported as obese. In the evaluable immunogenicity population (regardless of evidence of prior infection), 11/204 participants (5.4%) were baseline positive for prior SARS-CoV-2 infection.

SARS-CoV-2 NT50 were compared between an immunogenicity subset of Phase 2/3 participants 2 through 4 years of age from Study 3 at 1 month after the 3-dose primary series and a randomly selected subset from Study 2 Phase 2/3 participants 16 through 25 years of age at 1 month after the 2-dose primary series, using a microneutralization assay against the reference strain (USA_WA1/2020). The primary immunobridging analyses compared the geometric mean titers (using a GMR) and the seroresponse (defined as achieving at least 4-fold rise in SARS-CoV-2 NT50 from before Dose 1) rates in the evaluable immunogenicity population of participants without evidence of prior SARS-CoV-2 infection up to 1 month after Dose 3 in participants 2 through 4 years of age and up to 1 month after Dose 2 in participants 16 through 25 years of age. The prespecified immunobridging criteria were met for both the GMR and the seroresponse difference (Table 30 and Table 31, respectively).

Table 30: SARS-CoV-2 GMTs (NT50) at 1 Month After Completion of Primary Vaccination – Immunobridging Subset - Participants 2 Through 4 Years of Age (Study 3) 1 Month After Dose 3 and Participants 16 Through 25 Years of Age (Study 2) 1 Month After Dose 2 – Without Evidence of SARS-CoV-2 Infection – Evaluable Immunogenicity Population

	Pfizer-BioNTech COVID-19 Vaccine		GMR (95%CI) (2 Through 4 Years of Age/16 Through 25 Years of Age)[d,e]
	3 mcg modRNA/Dose 2 Through 4 Years of Age (1 Month After Dose 3) n[a]=143	30 mcg modRNA/Dose 16 Through 25 Years of Age (1 Month After Dose 2) n[a]=170	
Assay	**GMT[c] (95% CI[c])**	**GMT[c] (95% CI[c])**	
SARS-CoV-2 neutralization assay - NT50 (titer)[f]	1535.2 (1388.2, 1697.8)	1180.0 (1066.6, 1305.4)	1.30 (1.13, 1.50)

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMT = geometric mean titer; LLOQ = lower limit of quantitation; NAAT = nucleic-acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Participants who had no serological or virological evidence [(up to 1 month after Dose 2 (Study 2) or 1 month after Dose 3 (Study 3) blood sample collection)] of past SARS-CoV-2 infection [(i.e., N-binding antibody [serum] negative at Dose 1, Dose 3 (Study 3) and 1 month after Dose 2 (Study 2) or 1 month after Dose 3 (Study 3), SARS-CoV-2 not detected by NAAT [nasal swab] at Dose 1, Dose 2, and Dose 3 (Study 3) study visits, and negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2 (Study 2) or 1 month after Dose 3 (Study 3) blood collection)] and had no medical history of COVID-19 were included in the analysis.

a. n = Number of participants with valid and determinate assay results for the specified assay at the given dose/sampling time point.
b. Protocol-specified timing for blood sample collection.
c. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.
d. GMRs and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titers ([2 through 4 years of age] - [16 through 25 years of age]) and the corresponding CI (based on the Student t distribution).
e. Immunobridging is declared if the lower bound of the 2-sided 95% CI for the GMR ratio is greater than 0.67 and the point estimate of the GMR is ≥0.8.
f. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

Table 31: Difference in Percentages of Participants with Seroresponse at 1 Month After Completion of Primary Vaccination – Immunobridging Subset – Participants 2 Through 4 Years of Age (Study 3) 1 Month after Dose 3 and Participants 16 Through 25 Years of Age (Study 2) 1 Month after Dose 2 Without Evidence of Infection – Evaluable Immunogenicity Population

	Pfizer-BioNTech COVID-19 Vaccine		
	3 mcg modRNA/Dose 2 Through 4 Years of Age (1 Month After Dose 3) N[a]=141	30 mcg modRNA/Dose 16 Through 25 Years of Age (1 Month After Dose 2) N[a]=170	Difference in Seroresponse Rates %[d] (95% CI[e]) (2 Through 4 Years of Age minus 16 Through 25 Years of Age)[f]
Assay	**n[b] (%) (95% CI[c])**	**n[b] (%) (95% CI[c])**	
SARS-CoV-2 neutralization assay - NT50 (titer)[g]	141 (100.0) (97.4, 100.0)	168 (98.8) (95.8, 99.9)	1.2 (-1.5, 4.2)

Abbreviations: LLOQ = lower limit of quantitation; NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein–binding; NT50 = 50% neutralizing titer 50; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Seroresponse is defined as achieving a ≥4-fold rise from baseline (before Dose 1). If the baseline measurement is below the LLOQ, a postvaccination assay result ≥4 × LLOQ is considered a seroresponse.

Note: Participants who had no serological or virological evidence (up to 1 month after Dose 2 [(Study 2) or 1 month after Dose 3 (Study 3) blood sample collection)[of past SARS-CoV-2 infection [(i.e., N-binding antibody [serum] negative at pre-Dose 1, pre-Dose 3 (Study 3) and 1 month after Dose 2 (Study 2) or 1 month after Dose 3 (Study 3), SARS-CoV-2 not detected by NAAT [nasal swab] at pre-Dose 1, pre-Dose 2, and pre-Dose 3 (Study 3) study visits, and negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2 (Study 2) or 1 month after Dose 3 (Study 3) blood collection)] and had no medical history of COVID-19 were included in the analysis.

a. N = number of participants with valid and determinate assay results both before vaccination and at 1 month after Dose 2. These values are the denominators for the percentage calculations.
b. n = Number of participants with seroresponse for the given assay at the given dose/sampling time point.
c. Exact 2-sided CI based on the Clopper and Pearson method.
d. Difference in proportions, expressed as a percentage ([2 through 4 years of age] – [16 through 25 years of age]).
e. 2-sided CI, based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.
f. Immunobridging is declared if the lower bound of the 2-sided 95% CI for the difference in proportions is greater than -10.0% provided that the immunobridging criteria based on GMR were met.
g. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

Using a non-validated fluorescence focus reduction neutralization test assay against the Omicron variant of SARS-CoV-2 (BA.1), the NT50 GMT at 1 month after Dose 3 among a subset of 34 study participants without evidence of prior SARS-CoV-2 infection (82.5 [95% CI: 55.4, 122.9]) was increased compared to the NT50 GMT before Dose 3 (14.0 [95% CI: 10.6, 18.5]).

Immunogenicity in Participants 6 Through 23 Months of Age After a 3-Dose Primary Series

Immunogenicity analyses have been performed in the immunobridging subset of 82 Study 3 participants 6 through 23 months of age without evidence of infection up to 1 month after Dose 3 based on a data cutoff date of April 29, 2022.

The evaluable immunogenicity population without prior evidence of SARS-CoV-2 infection up to 1 month after Dose 3 of Pfizer-BioNTech COVID-19 Vaccine was comprised of 82 participants 6 through 23 months of age. Most participants in this analysis population were White (72.0%), with 1.2% Black or African American participants, 13.4% Asian participants, and 12.2% multi-racial participants. There were 15.9% Hispanic/Latino participants. The median age was 16.0 months and 62.2% of participants were male. In the evaluable immunogenicity population (regardless of evidence of prior infection), 6/132 participants (4.5%) were baseline positive for prior SARS-CoV-2 infection.

SARS-CoV-2 NT50 1 month after the vaccination series were compared between an immunogenicity subset of Phase 2/3 participants 6 through 23 months of age from Study 3 and a randomly selected subset from Study 2 Phase 2/3 participants 16 through 25 years of age, using a microneutralization assay against the reference strain (USA_WA1/2020). The primary immunobridging analyses compared the geometric mean titers (using a GMR) and the seroresponse (defined as achieving at least 4-fold rise in SARS-CoV-2 NT50 from before Dose 1) rates in the evaluable immunogenicity population of participants without evidence of prior SARS-CoV-2 infection up to 1 month after Dose 3 in participants 6 through 23 months of age and up to 1 month after Dose 2 in participants 16 through 25 years of age. The prespecified immunobridging criteria were met for both the GMR and the seroresponse difference (Table 32 and Table 33, respectively).

Table 32: SARS-CoV-2 GMTs (NT50) at 1 Month After Completion of Primary Vaccination – Immunobridging Subset - Participants 6 Through 23 Months of Age (Study 3) 1 Month After Dose 3 and Participants 16 Through 25 Years of Age (Study 2) 1 Month After Dose 2 – Without Evidence of SARS-CoV-2– Evaluable Immunogenicity Population

	Pfizer-BioNTech COVID-19 Vaccine		
	3 mcg modRNA/Dose 6 Through 23 months of Age (1 Month After Dose 3) n[a]=82	30 mcg modRNA/Dose 16 Through 25 Years of Age (1 Month After Dose 2) n[a]=170	GMR (95%CI) (6 Through 23 months of Age/16 Through 25 Years of Age)[c,d]
Assay	**GMT[b] (95% CI[b])**	**GMT[b] (95% CI[b])**	
SARS-CoV-2 neutralization assay - NT50 (titer)[e]	1406.5 (1211.3, 1633.1)	1180.0 (1066.6, 1305.4)	1.19 (1.00, 1.42)

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMT = geometric mean titer; LLOQ = lower limit of quantitation; NAAT = nucleic-acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Participants who had no serological or virological evidence [(up to 1 month after Dose 2 (Study 2) or 1 month after Dose 3 (Study 3) blood sample collection)] of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Dose 1, Dose 3 (Study 3) and 1 month after Dose 2 (Study 2) or 1 month after Dose 3 (Study 3), SARS-CoV-2 not detected by NAAT [nasal swab] at Dose 1, Dose 2, and Dose 3 (Study 3) study visits, and negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2 (Study 2) or 1 month after Dose 3 (Study 3) blood collection)] and had no medical history of COVID-19 were included in the analysis.

a. n = Number of participants with valid and determinate assay results for the specified assay at the given dose/sampling time point.
b. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

c. GMRs and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titers ([6 through 23 months of age] - [16 through 25 years of age]) and the corresponding CI (based on the Student t distribution).
d. Immunobridging is declared if the lower bound of the 2-sided 95% CI for the GMR ratio is greater than 0.67 and the point estimate of the GMR is ≥0.8.
e. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

Table 33: Difference in Percentages of Participants with Seroresponse at 1 Month After Completion of Primary Vaccination – Immunobridging Subset – Participants 6 Through 23 months of Age (Study 3) 1 Month After Dose 3 and Participants 16 Through 25 Years of Age (Study 2) to 1 Month After Dose 2 Without Evidence of Infection – Evaluable Immunogenicity Population

	Pfizer-BioNTech COVID-19 Vaccine		Difference in Seroresponse Rates %[d] (95% CI[e]) (6 Through 23 months of Age minus 16 Through 25 Years of Age)[f]
	3 mcg modRNA/Dose 6 Through 23 months of Age (1 Month After Dose 3) N[a]=80	30 mcg modRNA/Dose 16 Through 25 Years of Age (1 Month After Dose 2) N[a]=170	
Assay	n[b] (%) (95% CI[c])	n[b] (%) (95% CI[c])	
SARS-CoV-2 neutralization assay - NT50 (titer)[g]	80 (100.0) (95.5, 100.0)	168 (98.8) (95.8, 99.9)	1.2 (-3.4, 4.2)

Abbreviations: LLOQ = lower limit of quantitation; NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein–binding; NT50 = 50% neutralizing titer 50; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Seroresponse is defined as achieving a ≥4-fold rise from baseline (before Dose 1). If the baseline measurement is below the LLOQ, a postvaccination assay result ≥4 × LLOQ is considered a seroresponse.
Note: Participants who had no serological or virological evidence [(up to 1 month after Dose 2 (Study 2) or 1 month after Dose 3 (Study 3) blood sample collection) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at pre-Dose 1, Dose 3 (Study 3) and 1 month after Dose 2 (Study 2) or 1 month after Dose 3 (Study 3), SARS-CoV-2 not detected by NAAT [nasal swab] at pre-Dose 1, pre-Dose 2, and pre-Dose 3 (Study 3) study visits, and negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2 (Study 2) or 1 month after Dose 3 (Study 3) blood collection)] and had no medical history of COVID-19 were included in the analysis.
a. N = number of participants with valid and determinate assay results both before vaccination and at 1 month after Dose 2. These values are the denominators for the percentage calculations.
b. n = Number of participants with seroresponse for the given assay at the given dose/sampling time point.
c. Exact 2-sided CI based on the Clopper and Pearson method.
d. Difference in proportions, expressed as a percentage ([6 through 23 months of age] – [16 through 25 years of age]).
e. 2-sided CI, based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.
f. Immunobridging is declared if the lower bound of the 2-sided 95% CI for the difference in proportions is greater than -10.0% provided that the immunobridging criteria based on GMR were met.
g. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

Using a non-validated fluorescence focus reduction neutralization test assay against the Omicron variant of SARS-CoV-2 (BA.1), the NT50 GMT at 1 month after Dose 3 among a subset of 32 study participants without evidence of prior SARS-CoV-2 infection (127.5 [95% CI: 90.2, 180.1]) was increased compared to the NT50 GMT before Dose 3 (16.3 [95% CI: 12.8, 20.8]).

Efficacy in Participants 6 Months Through 4 Years of Age After a 3-Dose Primary Series

A descriptive efficacy analysis of Study 3 was performed across the combined population of participants 6 months through 4 years of age based on PCR-confirmed COVID-19 cases among 873 participants in the Pfizer-BioNTech COVID-19 Vaccine group and 381 participants in the placebo group (2:1 randomization) who received 3 doses of study intervention during the blinded follow-up period when the Omicron variant of SARS-CoV-2 (BA.2) was the predominant variant in circulation (data cutoff date of June 17, 2022).

The evaluable efficacy population without prior evidence of SARS-CoV-2 infection up to 7 days after Dose 3 of Pfizer-BioNTech COVID-19 Vaccine was comprised of 873 vaccine recipients and 381 placebo recipients 6 months through 4 years of age. Most vaccine recipients in this analysis population were White (76.3%), with 3.4% Black or African American participants, 10.0% Asian participants, and 10.1% who identified as multi-racial, other or not reported. There were 11.2% Hispanic/Latino vaccine recipients. Among the vaccine recipients, 51.1% were female. The median age was 16.0 months in vaccine recipients 6 through 23 months of age and the median age was 3.0 years in vaccine recipients 2 through 4 years of age. In the evaluable efficacy population, 8.7% of vaccine recipients had one or more comorbidities that increase the risk of severe COVID-19 as described in the Morbidity and Mortality Weekly Report (MMWR) 69(32);1081-8 and/or obesity (BMI ≥95th percentile) for participants 2 through 4 years of age. Between participants who received Pfizer-BioNTech COVID-19 Vaccine and those who received placebo, there were no notable differences in demographics.

The median dose interval between Dose 2 and Dose 3 was 13.4 weeks (range 8 to 33 weeks) among participants 6 through 23 months of age and 10 weeks (range 8 to 34 weeks) among participants 2 through 4 years of age who received Pfizer-BioNTech COVID-19 Vaccine. The median length of blinded follow-up for efficacy after Dose 3 was 1.7 months for participants 6 through 23 months of age and 2.1 months for participants 2 through 4 years of age in the Dose 3 Evaluable Efficacy Population who received Pfizer-BioNTech COVID-19 Vaccine or placebo.

The vaccine efficacy results after Dose 3 in participants 6 months through 4 years of age are presented in Table 34.

Table 34: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 3 – Blinded Follow-Up Period – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 3 – Phase 2/3 – 6 Months Through 4 Years of Age – Evaluable Efficacy (3-Dose) Population

First COVID-19 occurrence from 7 days after Dose 3 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**Pfizer-BioNTech COVID-19 Vaccine 3 mcg modRNA/Dose Na=873 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=381 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
6 months through 4 years[e]	13 0.124 (794)	21 0.054 (351)	73.2 (43.8, 87.6)
2 through 4 years	9 0.081 (498)	13 0.033 (204)	71.8 (28.6, 89.4)
6 through 23 months	4 0.042 (296)	8 0.020 (147)	75.8 (9.7, 94.7)
First COVID-19 occurrence from 7 days after Dose 3 in participants with or without evidence of prior SARS-CoV-2 infection			
Subgroup	**Pfizer-BioNTech COVID-19 Vaccine 3 mcg modRNA/Dose Na=1294 Cases n1b Surveillance Timec (n2d)**	**Placebo Na=612 Cases n1b Surveillance Timec (n2d)**	**Vaccine Efficacy % (95% CIe)**
6 months through 4 years[e]	14 0.149 (981)	23 0.067 (459)	72.5 (44.3, 86.9)
2 through 4 years	10 0.100 (639)	15 0.044 (286)	70.7 (30.3, 88.2)
6 through 23 months	4 0.048 (342)	8 0.023 (173)	76.2 (11.1, 94.8)

Abbreviations: NAAT = nucleic acid amplification test; N-binding = SARS-CoV-2 nucleoprotein–binding; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting; inability to eat/poor feeding).

* Participants who had no serological or virological evidence (prior to 7 days after receipt of Dose 3) of past SARS-CoV-2 infection (i.e., negative N-binding antibody [serum] result at Dose 1, 1 month post-Dose 2 (if available), Dose 3 (if available) visits, SARS-CoV-2 not detected by NAAT [nasal swab] at Dose 1, Dose 2, and Dose 3 study visits, and a negative NAAT [nasal swab] result at any unscheduled visit prior to 7 days after receipt of Dose 3) and had no medical history of COVID-19 were included in the analysis.

a. N = number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 3 to the end of the surveillance period.

d. n2 = Number of participants at risk for the endpoint.
e. Two-sided 95% confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

Among participants 6 months through 4 years of age, severe COVID-19 case criteria were fulfilled after Dose 3 in 1 placebo recipient in the 6 through 23-month age group. This case occurred 44 days after Dose 3, based on a single criterion (increased heart rate) and did not require hospitalization. There were no cases of multisystem inflammatory syndrome in children reported through the June 17, 2022 data cutoff date.

14.6 Immunogenicity of Pfizer-BioNTech COVID-19 Vaccine Administered as a First Booster Dose Following a Primary Series of Pfizer-BioNTech COVID-19 Vaccine in Participants 18 Through 55 Years of Age

Effectiveness of a single and additional doses of Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) was based on an assessment of NT50 against SARS-CoV-2 (USA_WA1/2020). In Study 2, analyses of NT50 1 month after the booster dose compared to 1 month after the primary series in individuals 18 through 55 years of age who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after the booster vaccination demonstrated noninferiority for both GMR and difference in seroresponse rates. Seroresponse for a participant was defined as achieving a ≥4-fold rise in NT50 from baseline (before primary series). These analyses are summarized in Table 35 and Table 36.

Table 35: Geometric Mean 50% Neutralizing Titer (SARS-CoV-2 USA_WA1/2020) – Comparison of 1 Month After Booster Dose to 1 Month After Primary Series – Participants 18 Through 55 Years of Age Without Evidence of Infection up to 1 Month After Booster Dose* – Booster Dose Evaluable Immunogenicity Population±

Assay	n[a]	1 Month After Booster Dose GMT[b] (95% CI[b])	1 Month After Primary Series GMT[b] (95% CI[b])	1 Month After Booster Dose/ 1 Month After Primary Series GMR[c] (97.5% CI[c])	Met Noninferiority Objective[d] (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)[e]	212	2466.0 (2202.6, 2760.8)	750.6 (656.2, 858.6)	3.29 (2.77, 3.90)	Y

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMT = geometric mean titer; LLOQ = lower limit of quantitation; N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; Y/N = yes/no.
Note: Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).
* Participants who had no serological or virological evidence (up to 1 month after receipt of a booster dose of Pfizer-BioNTech COVID-19 Vaccine) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative and SARS-CoV-2 not detected by NAAT [nasal swab]) and had a negative NAAT (nasal swab) at any unscheduled visit up to 1 month after the booster dose were included in the analysis.
± All eligible participants who had received 2 doses of Pfizer-BioNTech COVID-19 Vaccine as initially randomized, with Dose 2 received within the predefined window (within 19 to 42 days after Dose 1), received a booster dose of Pfizer-BioNTech COVID-19 Vaccine, had at least 1 valid and determinate immunogenicity result after booster dose from a blood collection within an appropriate window (within 28 to 42 days after the booster dose), and had no other important protocol deviations as determined by the clinician.

a. n = Number of participants with valid and determinate assay results at both sampling time points within specified window.
b. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.
c. GMRs and 2-sided 97.5% CIs were calculated by exponentiating the mean differences in the logarithms of the assay and the corresponding CIs (based on the Student t distribution).
d. Noninferiority is declared if the lower bound of the 2-sided 97.5% CI for the GMR is >0.67 and the point estimate of the GMR is ≥0.80.
e. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

Table 36: Seroresponse Rate for 50% Neutralizing Titer (SARS-CoV-2 USA_WA1/2020) – Comparison of 1 Month After Booster Dose to 1 Month After Primary Series – Participants 18 Through 55 Years of Age Without Evidence of Infection up to 1 Month After Booster Dose* – Booster Dose Evaluable Immunogenicity Population±

Assay	N[a]	1 Month After Booster Dose n[b] % (95% CI[c])	1 Month After Primary Series n[b] % (95% CI[c])	Difference (1 Month After Booster Dose - 1 Month After Primary Series) %[d] (97.5% CI[e])	Met Noninferiority Objective[f] (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)[g]	200	199 99.5 (97.2, 100.0)	196 98.0 (95.0, 99.5)	1.5 (-0.7, 3.7)	Y

Abbreviations: CI = confidence interval; LLOQ = lower limit of quantitation; N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; Y/N = yes/no.
Note: Seroresponse is defined as achieving a ≥4-fold rise from baseline (before Dose 1). If the baseline measurement is below the LLOQ, a postvaccination assay result ≥4 × LLOQ is considered a seroresponse.
Note: Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).
* Participants who had no serological or virological evidence (up to 1 month after receipt of booster vaccination) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative and SARS-CoV-2 not detected by NAAT [nasal swab]) and had a negative NAAT (nasal swab) at any unscheduled visit up to 1 month after booster vaccination were included in the analysis.
± All eligible participants who had received 2 doses of Pfizer-BioNTech COVID-19 Vaccine as initially randomized, with Dose 2 received within the predefined window (within 19 to 42 days after Dose 1), received a booster dose of Pfizer-BioNTech COVID-19 Vaccine, had at least 1 valid and determinate immunogenicity result after booster dose from a blood collection within an appropriate window (within 28 to 42 days after the booster dose), and had no other important protocol deviations as determined by the clinician.
a. N = number of participants with valid and determinate assay results for the specified assay at baseline, 1 month after Dose 2 and 1 month after the booster dose within specified window. These values are the denominators for the percentage calculations.
b. n = Number of participants with seroresponse for the given assay at the given dose/sampling time point.
c. Exact 2-sided CI based on the Clopper and Pearson method.
d. Difference in proportions, expressed as a percentage (1 month after booster dose – 1 month after Dose 2).
e. Adjusted Wald 2-sided CI for the difference in proportions, expressed as a percentage.
f. Noninferiority is declared if the lower bound of the 2-sided 97.5% CI for the percentage difference is > -10%.
g. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on

Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

14.7 Immunogenicity of Pfizer-BioNTech COVID-19 Vaccine Booster Dose Following Pfizer-BioNTech COVID-19 Vaccine Primary Series in Participants 5 Through 11 Years of Age

In Study 3, immunogenicity of a booster dose administered at 7 to 9 months after the second primary series dose was evaluated in 67 study participants 5 through 11 years of age who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after the booster dose. Using a microneutralization assay against the reference strain of SARS-CoV-2 (USA_WA1/2020), the NT50 GMT at 1 month after the booster dose (2720.9 [95% CI: 2280.1, 3247.0]) was increased compared to before the booster dose (271.0 [95% CI: 229.1, 320.6]). Using a non-validated fluorescence focus reduction neutralization test assay against the Omicron variant of SARS-CoV-2 (B.1.1.529), the NT50 GMT at 1 month after the booster dose among a subset of 17 study participants (614.4 [95% CI: 410.7, 919.2]) was increased compared to the NT50 GMT at 1 month after dose 2 among a subset of 29 study participants (27.6 [95% CI: 22.1, 34.5]).

14.8 Immunogenicity of the Pfizer-BioNTech COVID-19 Vaccine Booster Dose Following Primary Vaccination with Another Authorized or Approved COVID-19 Vaccine

Effectiveness of a Pfizer-BioNTech COVID-19 Vaccine booster dose (30 mcg modRNA) in individuals who completed primary vaccination with another authorized or approved COVID-19 Vaccine (heterologous booster dose) is inferred from immunogenicity data supporting effectiveness of a Pfizer-BioNTech COVID-19 Vaccine booster dose administered following completion of Pfizer-BioNTech COVID-19 Vaccine primary series and from immunogenicity data from an independent NIH study Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States that evaluated a heterologous booster dose of the Pfizer-BioNTech COVID-19 Vaccine. In this study, participants 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 1 of 3 vaccines: Moderna COVID-19 Vaccine, Janssen COVID-19 Vaccine, or Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA). 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 Pfizer-BioNTech COVID-19 Vaccine was demonstrated regardless of the vaccine used for primary vaccination.

14.9 Immunogenicity of Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) Administered as a Booster (Fourth Dose) in Individuals 6 Months Through 4 Years of Age

In Study 6, a subset of 60 participants 6 months through 4 years of age received a booster dose (fourth dose) of Pfizer-BioNTech COVID-19 Vaccine, Bivalent (3 mcg modRNA) after receiving 3 prior doses of Pfizer-BioNTech COVID-19 Vaccine (3 mcg modRNA). Neutralizing antibody levels following the fourth dose are presented in Table 37. Data from a subset of participants 6 months through 4 years of age in Study 3 who received 3 doses of Pfizer-BioNTech COVID-19 Vaccine (3 mcg modRNA) are included as a reference. There were no formal statistical comparisons of the immune response between subsets from the two studies.

Table 37: Study 6 – Geometric Mean Titers – Participants With or Without Evidence of Infection* – 6 Months Through 4 Years of Age – Evaluable Immunogenicity Population

SARS-CoV-2 Neutralization Assay	Age Group	Sampling Time Point[a]	Study 6 Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original/Omicron BA.4/BA.5) 3 mcg modRNA Dose 4 and 1 Month After Dose 4		Study 3 Pfizer-BioNTech COVID-19 Vaccine 3 mcg modRNA Dose 3 and 1 Month After Dose 3	
			n[b]	GMT[c] (95% CI[c])	n[b]	GMT[c] (95% CI[c])
Omicron BA.4/BA.5 - NT50 (titer)[f]	6 through 23 months	Pre-vaccination	21	243.9 (115.3, 516.1)	23	96.0 (55.3, 166.8)
		1 month	23	2011.4 (1141.3, 3544.9)	23	625.6 (365.7, 1070.5)
	2 through 4 years	Pre-vaccination	33	165.6 (88.3, 310.5)	31	56.1 (38.0, 82.7)
		1 month	35	1514.9 (882.2, 2601.5)	31	595.0 (370.5, 955.6)
Reference strain - NT50 (titer)[f]	6 through 23 months	Pre-vaccination	22	2491.2 (1432.0, 4333.8)	22	981.6 (503.5, 1913.7)
		1 month	23	8737.2 (5959.6, 12809.5)	23	9221.7 (6734.0, 12628.3)
	2 through 4 years	Pre-vaccination	35	2802.7 (1795.7, 4374.3)	31	657.9 (421.5, 1026.9)
		1 month	35	10448.3 (7685.1, 14205.1)	30	8933.3 (6388.0, 12492.9)

Abbreviations: GMT = geometric mean titer; LLOQ = lower limit of quantitation; N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test.
NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

* Included all participants regardless of SARS-CoV-2 infection status prior to or after vaccination.

a. Protocol-specified timing for blood sample collection.

b. n = Number of participants with valid and determinate assay results for the specified assay at the given sampling time point.

c. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

d. For Study 6: positive N-binding antibody result at Dose 4 visit, positive NAAT result at Dose 4 visit, or medical history of COVID-19. For Study 3: positive N-binding antibody result at Dose 1, 1-month post-Dose 2 (if available), or Dose 3 visits, positive NAAT result at Dose 1, Dose 2, Dose 3, or any unscheduled illness visit up to Dose 3 visit, or medical history of COVID-19.

e. For Study 6: negative N-binding antibody result at Dose 4 visit, negative NAAT result at Dose 4 visit, and no medical history of COVID-19. For Study 3: negative N-binding antibody result at Dose 1, 1-month post-Dose 2 (if available), and Dose 3 visits, negative NAAT result at Dose 1, Dose 2, Dose 3, and any unscheduled illness visits up to Dose 3 visit, and no medical history of COVID-19.

f. SARS-CoV-2 NT50 were determined using a validated 384-well assay platform (original strain [USA-WA1/2020, isolated in January 2020] and Omicron B.1.1.529 subvariant BA.4/BA.5).

14.10 Immunogenicity of the Bivalent Vaccine (Original and Omicron BA.1) Administered as a Second Booster Dose

In an analysis of a subset from Study 4, a total of 610 participants greater than 55 years of age who had previously received a 2-dose primary series and 1 booster dose with Pfizer-BioNTech COVID-19 Vaccine received 1 of the following as a second booster dose: Pfizer-BioNTech COVID-19 Vaccine or bivalent vaccine (Original and Omicron BA.1). GMRs and seroresponse rates were evaluated at 1 month after vaccination with the bivalent vaccine (Original and Omicron BA.1). The bivalent vaccine (Original and Omicron BA.1) booster dose was administered 4.7 to 11.5 months (median 6.3 months) after the first booster dose. The Pfizer-BioNTech COVID-19 Vaccine booster dose was administered 5.3 to 13.1 months (median 6.3 months) after the first booster dose.

The primary objective of the study was to assess superiority with respect to level of NT50 and noninferiority with respect to seroresponse rate of the anti-Omicron BA.1 immune response induced by a dose of the bivalent vaccine (Original and Omicron BA.1) relative to the response elicited by a dose of Pfizer-BioNTech COVID-19 Vaccine given as a second booster dose in participants greater than 55 years of age.

A secondary objective of the study was to assess noninferiority with respect to level of NT50 to the Original SARS-COV-2 strain induced by a dose of the bivalent vaccine (Original and Omicron BA.1) relative to the response elicited by a dose of Pfizer-BioNTech COVID-19 Vaccine given as a second booster dose. A comparison of seroresponse rates to the Original strain was descriptive.

Superiority of the anti-Omicron BA.1 NT50 for the bivalent vaccine (Original and Omicron BA.1) relative to Pfizer-BioNTech COVID-19 Vaccine was met, as the lower bound of the 2-sided 95% CI for GMR was >1. Noninferiority of the anti-Original NT50 for the bivalent vaccine (Original and Omicron BA.1) relative to Pfizer-BioNTech COVID-19 Vaccine was met, as the lower bound of the 2-sided 95% CI for GMR was >0.67 and the point estimate of the GMR was ≥0.8 (Table 38).

Non-inferiority of the seroresponse rate to the Omicron BA.1 variant for the bivalent vaccine (Original and Omicron BA.1) relative to Pfizer-BioNTech COVID-19 Vaccine was met as the lower limit of the 2-sided 95% CI for the difference in percentages of participants with seroresponse is >-5% (Table 38). A descriptive summary of seroresponse to the Original strain is also included in Table 39.

Table 38: Study 4 - Geometric Mean Ratios – Participants Without Evidence of Infection Up to 1 Month After the Second Booster Dose – Immunogenicity Subset – Participants Greater Than 55 Years of Age – Evaluable Immunogenicity Population

Assay	Vaccine Group (as randomized)	Sampling Time Point[a]	N[b]	GMT (95% CI[c])	GMR (95% CI[d])
SARS-CoV-2 neutralization assay - Omicron BA.1 - NT50 (titer)[e]	Pfizer-BioNTech COVID-19 Vaccine	1 month	163	455.8 (365.9, 567.6)	
	Bivalent Vaccine (Original and Omicron BA.1)	1 month	178	711.0 (588.3, 859.2)	1.56 (1.17, 2.08)
SARS-CoV-2 neutralization assay - Original strain - NT50 (titer)[e]	Pfizer-BioNTech COVID-19 Vaccine	1 month	182	5998.1 (5223.6, 6887.4)	
	Bivalent Vaccine (Original and Omicron BA.1)	1 month	186	5933.2 (5188.2, 6785.2)	0.99 (0.82, 1.20)

Abbreviations: GMR = geometric mean ratio; GMT = geometric mean titer; LLOQ = lower limit of quantitation; N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Immunogenicity subset = a random sample of 230 participants in each vaccine group.
Note: Participants who had no serological or virological evidence (prior to the 1-month post–study vaccination blood sample collection) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] result negative at the study vaccination and the 1-month post–study vaccination visits, negative NAAT [nasal swab] result at the study vaccination visit, and any unscheduled visit prior to the 1-month post–study vaccination blood sample collection) and had no medical history of COVID-19 were included in the analysis.

a. Protocol-specified timing for blood sample collection.
b. n = number of participants with valid and determinate assay results for the specified assay at the given sampling time point.
c. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.
d. GMRs and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titers (vaccine group in the corresponding row - Pfizer-BioNTech COVID-19 Vaccine) and the corresponding CI (based on the Student t distribution). Superiority for anti-Omicron BA.1 immune response is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 1 after satisfying multiplicity adjustment. Noninferiority for anti-Original strain is declared if the lower limit of the 2-sided 95% CI for the GMR is greater than 0.67 (1.5-fold criterion) and the point estimate of the GMR is ≥0.8, after satisfying multiplicity adjustment.
e. SARS-CoV-2 NT50 were determined using a validated 384-well assay platform (original strain [USA-WA1/2020, isolated in January 2020] and Omicron B.1.1.529 subvariant BA.1).

Table 39: Study 4 - Number (%) of Participants Achieving Seroresponse – Participants Without Evidence of Infection Up to 1 Month After the Second Booster Dose – Immunogenicity Subset – Participants Greater Than 55 Years of Age – Evaluable Immunogenicity Population

Assay	Vaccine Group (as randomized)	Sampling Time Point[a]	N[b]	n[c] (%) (95% CI[d])	Difference %[e] (95% CI[f])
SARS-CoV-2 neutralization assay - Omicron BA.1 - NT50 (titer)[g]	Pfizer-BioNTech COVID-19 Vaccine	1 month	149	85 (57.0) (48.7, 65.1)	
	Bivalent Vaccine (Original and Omicron BA.1)	1 month	169	121 (71.6) (64.2, 78.3)	14.6 (4.0, 24.9)
SARS-CoV-2 neutralization assay - Original strain - NT50 (titer)[g]	Pfizer-BioNTech COVID-19 Vaccine	1 month	179	88 (49.2) (41.6, 56.7)	
	Bivalent Vaccine (Original and Omicron BA.1)	1 month	186	93 (50.0) (42.6, 57.4)	

Abbreviations: LLOQ = lower limit of quantitation; N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Note: Immunogenicity subset = a random sample of 230 participants in each vaccine group.
Note: Seroresponse is defined as achieving ≥4-fold rise from baseline (before the second booster dose). If the baseline measurement is below the LLOQ, the postvaccination measure of ≥4 × LLOQ is considered a seroresponse.
Note: Participants who had no serological or virological evidence (prior to the 1-month post–study vaccination blood sample collection) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] result negative at the study vaccination and the 1-month post–study vaccination visits, negative NAAT [nasal swab] result at the study vaccination visit, and any unscheduled visit prior to the 1-month post–study vaccination blood sample collection) and had no medical history of COVID-19 were included in the analysis.

a. Protocol-specified timing for blood sample collection.
b. N = Number of participants with valid and determinate assay results for the specified assay at both the pre-vaccination time point and the given sampling time point. This value is the denominator for the percentage calculation.
c. n = Number of participants with seroresponse at 1 month after vaccination for the given assay.
d. Exact 2-sided CI based on the Clopper and Pearson method.

e. Difference in proportions, expressed as a percentage (vaccine group in the corresponding row - Pfizer-BioNTech COVID-19 Vaccine.
f. 2-sided CI based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage. Noninferiority for anti-Omicron BA.1 seroresponse is declared if the lower bound of the 2-sided 95% CI for the difference is greater than -5% after satisfying multiplicity adjustment.
g. SARS-CoV-2 NT50 were determined using a validated 384-well assay platform (original strain [USA-WA1/2020, isolated in January 2020] and Omicron B.1.1.529 subvariant BA.1).

14.11 Effectiveness of a Single Dose of Pfizer-BioNTech COVID-19 Vaccine in Individuals 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).

Powell et al. conducted an observational test-negative study including symptomatic individuals aged 12 to 17 years of age with SARS-CoV-2 polymerase-chain-reaction (PCR) testing results in England from August 9, 2021 to March 31, 2022 (Powell et al. *Protection against symptomatic infection with delta (B.1.617.2) and omicron (B.1.1.529) BA.1 and BA.2 SARS-CoV-2 variants after previous infection and vaccination in adolescents in England, August, 2021–March, 2022: a national, observational, test-negative, case-control study. Lancet Infectious Diseases. April 2023)*. Among 1,161,704 SARS-CoV-2 PCR tests linked to COVID-19 vaccination status, there were 390,467 SARS-CoV-2 PCR confirmed positive tests during Delta variant predominance and 212,433 SARS-CoV-2 positive tests during Omicron variants BA.1 and BA.2 predominance. Among adolescents who had received only 1 dose of Pfizer-BioNTech COVID-19 Vaccine, those who had evidence of previous infection with Alpha, Delta, or Omicron variants had increased protection against symptomatic Omicron infection compared with those with no evidence of previous infection. At 2 to 14 weeks following 1 dose of Pfizer-BioNTech COVID-19 Vaccine, the estimated vaccine effectiveness was 18.8% (95% CI: 17.2%, 20.3%), 81.5% (95% CI: 80.0%, 82.9%), 78.8% (95% CI: 77.9, 79.5%), and 79.6% (95% CI: 44.9%, 92.4%) for individuals with no evidence of prior infection, and evidence of prior Alpha, Delta, and Omicron infection, respectively.

14.12 Immunogenicity of a Third Primary Series Dose in Individuals with Certain Kinds of Immunocompromise

From an independent report (*Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med),* a single arm study has been conducted in 101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously. A third dose of the Pfizer-BioNTech COVID-19 vaccine was administered to 99 of these individuals approximately 2 months after they had received a second dose. Among the 59 patients who had been seronegative before the third dose, 26 (44%) were seropositive at 4 weeks after the third dose. All 40 patients who had been seropositive before the third dose were still seropositive 4 weeks later. The prevalence of anti SARS-CoV-2 antibodies was 68% (67 of 99 patients) 4 weeks after the third dose.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5): multiple dose vials with maroon caps and labels with maroon borders

NDC 59267-0609-2	Carton of 10 multiple-dose vials
NDC 59267-0609-1	Multiple dose vial containing 10 doses of 0.2 mL (after dilution)

Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5): multiple dose vials with orange caps and labels with orange borders

NDC 59267-0565-2	Carton of 10 multiple-dose vials
NDC 59267-0565-1	Multiple dose vial containing 10 doses of 0.2 mL (after dilution)

Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5): multiple dose and single dose vials with gray caps and labels with gray borders

Single Dose Vials

NDC 59267-1404-2	Carton of 10 single dose vials
NDC 59267-1404-1	One vial contains 1 dose of 0.3 mL (Do Not Dilute)

Multiple Dose Vials

NDC 59267-0304-2	Carton of 10 multiple dose vials
NDC 59267-0304-1	Multiple dose vial containing 6 doses of 0.3 mL (Do Not Dilute)

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Do not refreeze thawed vials.

Vial Storage Prior to Use

Cartons of Pfizer-BioNTech COVID-19 Vaccine, Bivalent may arrive frozen at ultra-cold conditions in thermal containers with dry ice.

Once received, frozen vials may be immediately transferred to the refrigerator [2ºC to 8ºC (35ºF to 46ºF)], thawed and stored for up to 10 weeks. The 10-week refrigerated expiry date should be recorded on the carton at the time of transfer. Cartons of multiple dose vials with maroon caps and labels with maroon borders and single dose vials with gray caps and labels with gray borders may take up to 2 hours to thaw at this temperature. Cartons of multiple dose vials with orange caps and labels with orange borders may take up to 4 hours to thaw at this temperature. Cartons of multiple dose vials with gray caps and labels with gray borders may take up to 6 hours to thaw at this temperature.

Alternatively, frozen vials may be stored in an ultra-low temperature freezer at -90ºC to -60ºC (-130ºF to -76ºF) for up to 18 months from the date of manufacture. Do not store vials at -25°C to -15°C (-13°F to 5°F). Once vials are thawed, they should not be refrozen.

If cartons of Pfizer-BioNTech COVID-19 Vaccine, Bivalent are received at 2°C to 8°C (35ºF to 46ºF), they should be stored at 2°C to 8°C (35ºF to 46ºF). Check that the carton has been updated to reflect the 10-week refrigerated expiry date.

Regardless of storage condition, the vaccine should not be used after 18 months from the date of manufacture printed on the vial and cartons.

Vial Storage During Use

If not previously thawed at 2ºC to 8ºC (35ºF to 46ºF), allow Pfizer-BioNTech COVID-19 Vaccine, Bivalent single dose vials or multiple dose vials to thaw at room temperature [up to 25ºC (77ºF)] for 30 minutes.

Pfizer-BioNTech COVID-19 Vaccine, Bivalent may be stored at room temperature [8°C to 25°C (46°F to 77°F)] for a total of 12 hours prior to the first puncture. After first puncture, the multiple dose vials should be held between 2ºC to 25°C (35°F to 77°F). Multiple dose vials should be discarded 12 hours after first puncture.

Transportation of Vials

If local redistribution is needed, single dose vials and multiple dose vials may be transported at -90°C to -60°C (-130°F to -76°F) or 2°C to 8°C (35°F to 46°F).

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, visit the website or call the telephone number provided below.

Website	Telephone number
www.cvdvaccine.com	1-877-829-2619 (1-877-VAX-CO19)

This Full EUA Prescribing Information may have been updated. For the most recent Full EUA Prescribing Information, please see www.cvdvaccine.com.

BIONTECH
Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10001

LAB-1571-0.3

Revised: 18 April 2023