FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE (VACCINATION PROVIDERS)

EMERGENCY USE AUTHORIZATION (EUA)

PFIZER-BIONTECH COVID-19 VACCINE, BIVALENT (ORIGINAL AND OMICRON BA.4/BA.5)

BOOSTER DOSE FOR 5 THROUGH 11 YEARS OF AGE DILUTE BEFORE USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product, Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) for active immunization to prevent COVID-19 in individuals 5 years 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. It is supplied in multiple dose vials with orange caps and labels with orange borders.

DILUTE PRIOR TO USE.

Pfizer-BioNTech COVID-19 Vaccine, Bivalent is authorized for use in individuals 5 through 11 years of age and older as a single booster dose administered at least 2 months after either:

- **completion of primary vaccination with any authorized or approved COVID-19 vaccine, or**
- **receipt of the most recent booster dose with any authorized or approved monovalent[1] COVID-19 vaccine.**

This Fact Sheet pertains only to Pfizer-BioNTech COVID-19 Vaccine, Bivalent supplied in a multiple dose vial with an orange cap and a label with an orange border, which MUST BE DILUTED PRIOR TO USE. The vial labels state: Age 5y to <12y. The carton labels state: For age 5 years to <12 years.

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

Pfizer-BioNTech COVID-19 Vaccine, Bivalent, which is supplied in a multiple dose vial with an orange cap and a label with an orange border, should not be used in individuals 6 months through 4 years of age or 12 years of age and older.[2]

SUMMARY OF INSTRUCTIONS FOR COVID-19 VACCINATION PROVIDERS

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. See "MANDATORY REQUIREMENTS FOR PFIZER-BIONTECH COVID-19 VACCINE, BIVALENT ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION" for reporting requirements.

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

See this Fact Sheet for instructions for preparation and administration. This Fact Sheet may have been updated. For the most recent Fact Sheet, please see www.cvdvaccine.com.

For information on clinical trials that are testing the use of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent for active immunization to prevent COVID-19, please see www.clinicaltrials.gov.

DESCRIPTION OF COVID-19

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-CoV-2, that appeared in late 2019. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have reported a wide range of symptoms, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

[2] Different presentations of Pfizer-BioNTech COVID-19 Vaccine, Bivalent are available. Pfizer-BioNTech COVID-19 Vaccine, Bivalent, supplied in multiple dose vials with maroon caps and labels with maroon borders, is available for use as a third dose of the primary series in individuals 6 months through 4 years of age. Pfizer-BioNTech COVID-19 Vaccine, Bivalent, supplied in single dose and multiple dose vials with gray caps and labels with gray borders, is available for use as a single booster dose in individuals 12 years of age and older.

DOSAGE AND ADMINISTRATION

The storage, preparation, and administration information in this Fact Sheet apply to the Pfizer-BioNTech COVID-19 Vaccine, Bivalent, which is supplied in multiple dose vials with orange caps and labels with orange borders.

MUST BE DILUTED PRIOR TO USE.

Pfizer-BioNTech COVID-19 Vaccine, Bivalent Multiple Dose Vial with Orange Cap and a Label with an Orange Border

Age Range	Dilution Information	Doses Per Vial After Dilution	Dose Volume
5 through 11 years (Vial labels state: Age 5y to <12y)	Dilute with 1.3 mL sterile 0.9% Sodium Chloride Injection, USP prior to use	10	0.2 mL

Storage and Handling

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 multiple dose vials with orange caps and labels with orange borders 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. A carton of 10 vials may take up to 4 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 multiple dose vials with orange caps and labels with orange borders 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 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 dilution.

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.

Transportation of Vials

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

Dosing and Schedule

A single booster dose (0.2 mL) of Pfizer-BioNTech COVID-19 Vaccine, Bivalent may be administered at least 2 months after completion of primary vaccination with any authorized or approved COVID-19 vaccine or after receipt of the most recent booster dose with any authorized or approved monovalent COVID-19 vaccine.

Dose Preparation

Each vial **MUST BE DILUTED** before administering the vaccine.

Prior to Dilution

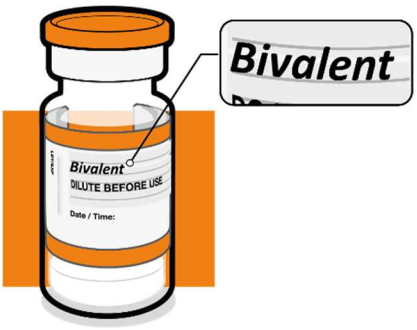
- The Pfizer-BioNTech COVID-19 Vaccine, Bivalent vials contain a frozen suspension that does not contain a preservative. Each vial must be thawed before dilution.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)].
- Refer to thawing and preparation instructions in the panels below.

Dilution

Dilute the vial contents using 1.3 mL of sterile 0.9% Sodium Chloride Injection, USP (not provided) to form the Pfizer-BioNTech COVID-19 Vaccine, Bivalent.

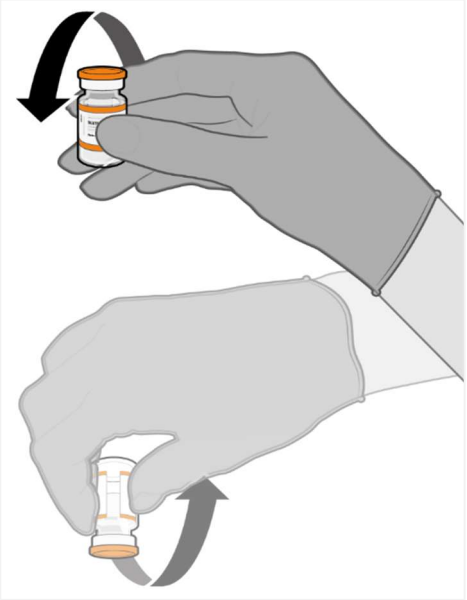
ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. This diluent is not packaged with the vaccine and must be sourced separately. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent. Do not add more than 1.3 mL of diluent.

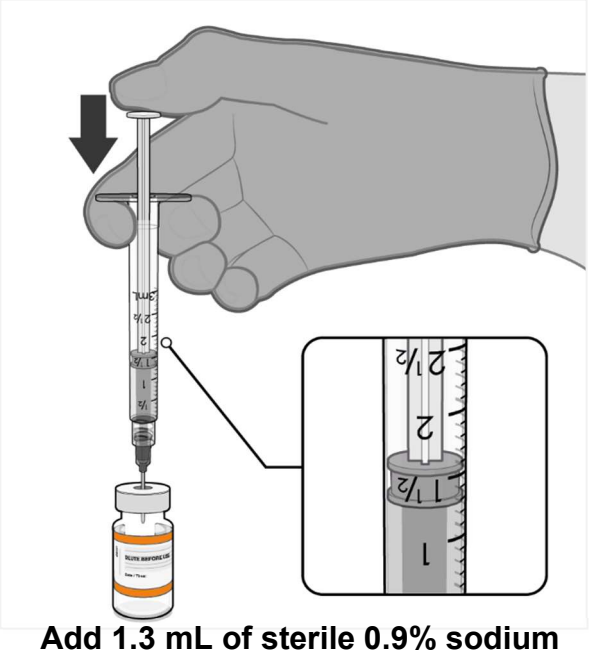
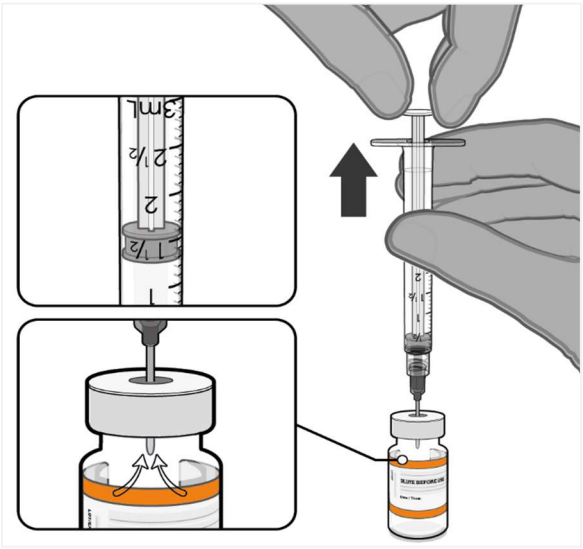
After dilution, 1 vial contains 10 doses of 0.2 mL.

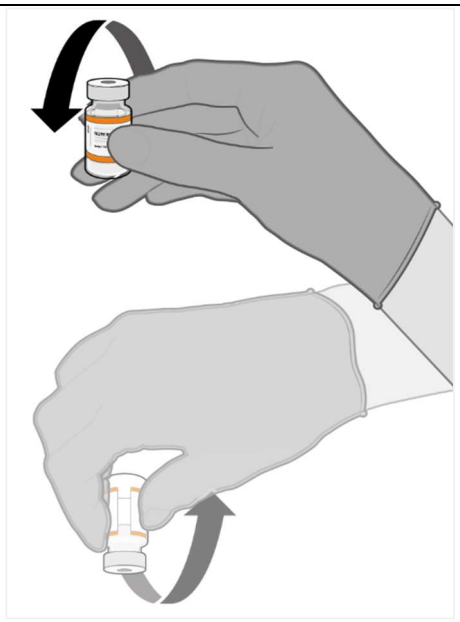
<table>
<tr><th colspan="2">Dilution and Preparation Instructions</th></tr>
<tr><td colspan="2">Pfizer-BioNTech COVID-19 Vaccine, Bivalent Vial with Orange Cap and Label with Orange Border –
VIAL VERIFICATION</td></tr>
<tr><td> 

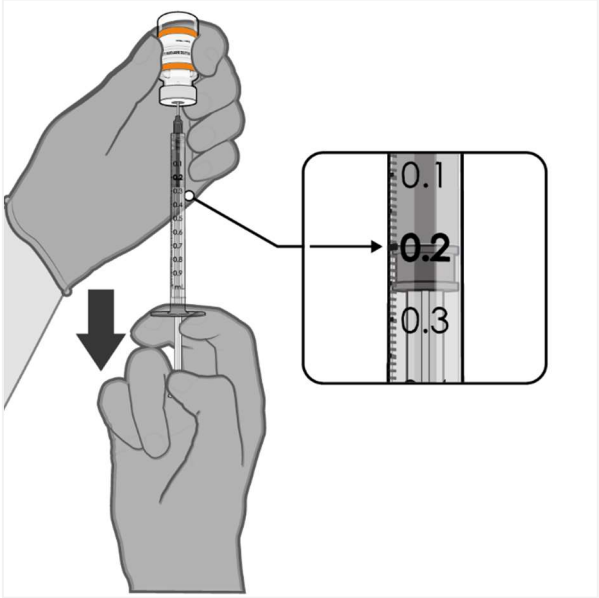
✓ Orange cap and label with orange border.</td><td>• Verify that the vial of Pfizer-BioNTech COVID-19 Vaccine, Bivalent:
○ has an orange cap and a label with an orange border,
○ states Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5), and
○ states “Age 5y to < 12y.”</td></tr>
<tr><td colspan="2">THAWING PRIOR TO DILUTION</td></tr>
<tr><td> 

Store in the refrigerator for up to 10 weeks prior to use.</td><td>• Thaw vial(s) of Pfizer-BioNTech COVID-19 Vaccine, Bivalent before use either by:
○ Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)].
▪ A carton of 10 vials may take up to 4 hours to thaw.
○ Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes.
• Thawed vials can be stored in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 10 weeks prior to use.
• Thawed vials may be stored at room temperature [up to 25ºC (77ºF)] for up to 12 hours prior to use.</td></tr>
</table>

Dilution and Preparation Instructions	
 **Gently × 10**	• Before dilution, mix by inverting vaccine vial gently 10 times. • <u>Do not shake</u>. • 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.

Dilution and Preparation Instructions	
DILUTION	
 **Add 1.3 mL of sterile 0.9% sodium chloride injection, USP.**	• Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent. • Using aseptic technique, withdraw 1.3 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Cleanse the vaccine vial stopper with a single-use antiseptic swab. • Add 1.3 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.
 **Pull back plunger to 1.3 mL to remove air from vial.**	• Equalize vial pressure before removing the needle from the vial by withdrawing 1.3 mL air into the empty diluent syringe.

Dilution and Preparation Instructions	
 **Gently × 10**	• 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.** **Use within 12 hours after dilution.**	• Record the date and time of dilution on the Pfizer-BioNTech COVID-19 Vaccine, Bivalent vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 12 hours after dilution.

Dilution and Preparation Instructions	
WITHRAWAL OF INDIVIDUAL 0.2 mL DOSES	
 **Withdraw 0.2 mL dose of vaccine.**	• 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. • Administer immediately. • 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.

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.

After withdrawing a single dose of 0.2 mL of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent, administer immediately.

Contraindications

Do not administer Pfizer-BioNTech COVID-19 Vaccine, Bivalent to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the Pfizer-BioNTech COVID-19 Vaccine or the Pfizer-BioNTech COVID-19 Vaccine, Bivalent *(see Full EUA Prescribing Information)*.

Warnings

Management of Acute Allergic Reactions

Appropriate medical treatment used 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).

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 receipt of the second primary series dose or first booster dose, with most booster doses likely administered at least 5 months after completing primary vaccination. For the Pfizer-BioNTech COVID-19 Vaccine, the observed risk is higher among adolescent males and adult males under 40 years of age than among females and older males, and 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).

Syncope

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

Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Pfizer-BioNTech COVID-19 Vaccine, Bivalent.

Limitation of Effectiveness

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

Adverse Reactions

The safety of a booster dose of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent is based on:

- safety data from a clinical study which evaluated a booster dose of Pfizer-BioNTech's bivalent COVID-19 vaccine (Original and Omicron BA.1), not authorized or approved, hereafter referred to as bivalent vaccine (Original and Omicron BA.1),
- safety data from clinical trials which evaluated primary and booster vaccination with the Pfizer-BioNTech COVID-19 Vaccine, and
- postmarketing safety data with the Pfizer-BioNTech COVID-19 Vaccine.

The safety data accrued with the bivalent vaccine (Original and Omicron BA.1) and with the Pfizer-BioNTech COVID-19 Vaccine are relevant to the Pfizer-BioNTech COVID-19 Vaccine, Bivalent because these vaccines are manufactured using the same process. The bivalent vaccine (Original and Omicron BA.1) contained 15 mcg of nucleoside-modified messenger RNA (modRNA) encoding the 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 lineage BA.1, for a total of 30 mcg modRNA per dose. This is the same total quantity of modRNA per dose as a dose of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent and as a dose of the Pfizer-BioNTech COVID-19 Vaccine authorized for primary vaccination in individuals 12 years of age and older (and previously, but no longer, authorized for booster vaccination in individuals 12 years of age and older).

Adverse Reactions in Clinical Trials

Adverse reactions in individuals 5 through 11 years of age following administration of a single booster dose of Pfizer-BioNTech COVID-19 Vaccine included injection site pain, fatigue, headache, muscle pain, injection site swelling, injection site redness, chills, fever, joint pain, diarrhea, lymphadenopathy, and vomiting *(see Full EUA Prescribing Information)*.

Adverse reactions in individuals greater than 55 years of age following administration of the bivalent vaccine (Original and Omicron BA.1) included pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, injection site redness, injection site swelling, fever, lymphadenopathy, nausea, and malaise.

Adverse Reactions Identified in Post Authorization Experience

Severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema), diarrhea, vomiting, pain in extremity (arm), syncope, and dizziness have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine.

Myocarditis and pericarditis have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine.

Additional adverse reactions, some of which may be serious, may become apparent with post authorization use of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent.

Use with Other Vaccines

There is no information on the co-administration of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent with other vaccines.

INFORMATION TO PROVIDE TO VACCINE RECIPIENTS/CAREGIVERS

As the vaccination provider, you must communicate to the recipient or their caregiver, information consistent with the "Fact Sheet for Recipients and Caregivers" (and provide a copy or direct the individual to the website www.cvdvaccine.com to obtain the Fact Sheet for Recipients and Caregivers) prior to the individual receiving each dose of Pfizer-BioNTech COVID-19 Vaccine, Bivalent, including:

- FDA has authorized the emergency use of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent which is not an FDA-approved vaccine.
- There is an option to accept or refuse Pfizer-BioNTech COVID-19 Vaccine, Bivalent.
- The significant known and potential risks and benefits of Pfizer-BioNTech COVID-19 Vaccine, Bivalent and the extent to which such risks and benefits are unknown.
- Information about available alternative vaccines and the risks and benefits of those alternatives.

For information on clinical trials that are testing the use of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent to prevent COVID-19, please see www.clinicaltrials.gov.

Provide a vaccination card to the recipient or their caregiver.

Provide the v-safe information sheet to vaccine recipients/caregivers and encourage vaccine recipients to participate in v-safe. V-safe is a new voluntary smartphone-based tool that uses text messaging and web surveys to check in with people who have been vaccinated to identify potential side effects after COVID-19 vaccination. V-safe asks questions that help CDC monitor the safety of COVID-19 vaccines. V-safe also provides dose reminders if needed and live telephone follow-up by CDC if participants report a significant health impact following COVID-19 vaccination. For more information, visit: www.cdc.gov/vsafe.

MANDATORY REQUIREMENTS FOR PFIZER-BIONTECH COVID-19 VACCINE, BIVALENT ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION[3]

In order to mitigate the risks of using this unapproved product under EUA and to optimize the potential benefit of Pfizer-BioNTech COVID-19 Vaccine, Bivalent, the following items are required. Use of unapproved Pfizer-BioNTech COVID-19 Vaccine, Bivalent for active immunization to prevent COVID-19 under this EUA is limited to the following (all requirements **must** be met):

1. Pfizer-BioNTech COVID-19 Vaccine, Bivalent is authorized for use in individuals 5 years of age and older.

2. The vaccination provider must communicate to the individual receiving the Pfizer-BioNTech COVID-19 Vaccine, Bivalent or their caregiver, information consistent with the "Fact Sheet for Recipients and Caregivers" prior to the individual receiving Pfizer-BioNTech COVID-19 Vaccine, Bivalent.

3. The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system.

4. The vaccination provider is responsible for mandatory reporting of the following to the Vaccine Adverse Event Reporting System (VAERS):
    - vaccine administration errors whether or not associated with an adverse event,
    - serious adverse events* (irrespective of attribution to vaccination),
    - cases of 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.

    Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html. For further assistance with reporting to VAERS call 1-800-822-7967. The reports should include the words "Pfizer-BioNTech COVID-19 Vaccine, Bivalent EUA" in the description section of the report.

5. The vaccination provider is responsible for responding to FDA requests for information about vaccine administration errors, adverse events, cases of myocarditis, cases of pericarditis, cases of 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 recipients.

[3] Vaccination providers administering COMIRNATY (COVID-19 Vaccine, mRNA) and Pfizer-BioNTech COVID-19 Vaccine must adhere to the same reporting requirements.

* 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 1 of the outcomes listed above.

OTHER ADVERSE EVENT REPORTING TO VAERS AND PFIZER INC.

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

ADDITIONAL INFORMATION

For general questions, visit the website or call the telephone number provided below.

To access the most recent Pfizer-BioNTech COVID-19 Vaccine, Bivalent Fact Sheets, please scan the QR code provided below.

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

AVAILABLE ALTERNATIVES

There may be clinical trials or availability under EUA of other COVID-19 vaccines for use as a booster dose, including bivalent vaccines that contain or encode the spike protein of the Omicron variant of SARS-CoV-2.

FEDERAL COVID-19 VACCINATION PROGRAM

This vaccine is being made available for emergency use exclusively through the CDC COVID-19 Vaccination Program (the Vaccination Program). Healthcare providers must enroll as providers in the Vaccination Program and comply with the provider requirements. Vaccination providers may not charge any fee for the vaccine and may not charge the vaccine recipient any out-of-pocket charge for administration. However, vaccination providers may seek appropriate reimbursement from a program or plan that covers COVID-19 vaccine administration fees for the vaccine recipient (private insurance, Medicare, Medicaid, Health Resources & Services Administration [HRSA] COVID-19 Uninsured Program for non-insured recipients). For information regarding provider requirements and enrollment in the CDC COVID-19 Vaccination Program, see https://www.cdc.gov/vaccines/covid-19/provider-enrollment.html.

Individuals becoming aware of any potential violations of the CDC COVID-19 Vaccination Program requirements are encouraged to report them to the Office of the Inspector General, U.S. Department of Health and Human Services, at 1-800-HHS-TIPS or https://TIPS.HHS.GOV.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of Health and Human Services (HHS) has declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19 pandemic. In response, FDA has issued an EUA for the unapproved product, Pfizer-BioNTech COVID-19 Vaccine, Bivalent for active immunization to prevent COVID-19.

FDA issued this EUA, based on Pfizer-BioNTech's request and submitted data.

For the authorized uses, although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that the Pfizer-BioNTech COVID-19 Vaccine, Bivalent may be effective for the prevention of COVID-19 in individuals as specified in the *Full EUA Prescribing Information*.

This EUA for the Pfizer-BioNTech COVID-19 Vaccine, Bivalent will end when the Secretary of HHS determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

For additional information about Emergency Use Authorization visit FDA at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.

The Countermeasures Injury Compensation Program

The Countermeasures Injury Compensation Program (CICP) is a federal program that has been created to help pay for related costs of medical care and other specific expenses to compensate people injured after use of certain medical countermeasures. Medical countermeasures are specific vaccines, medications, devices, or other items used to prevent, diagnose, or treat the public during a public health emergency or a security threat. For more information about CICP regarding the Pfizer-BioNTech COVID-19 Vaccine, Bivalent used to prevent COVID-19, visit www.hrsa.gov/cicp, email cicp@hrsa.gov, or call: 1-855-266-2427.

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

Pfizer
Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1543-2.3c

Revised: 8 December 22

END SHORT VERSION FACT SHEET
Long Version (Full EUA Prescribing Information) Begins On Next Page

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

PFIZER-BIONTECH COVID-19 VACCINE, BIVALENT (ORIGINAL AND OMICRON BA.4/BA.5)

FULL EMERGENCY USE AUTHORIZATION PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full emergency use authorization prescribing information are not listed.

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

1 AUTHORIZED USE

Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) is authorized for use under an Emergency Use Authorization (EUA) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 5 years of age and older.

This EUA Prescribing Information pertains only to Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5), hereafter referred to as Pfizer-BioNTech COVID-19 Vaccine, Bivalent, supplied in a multiple dose vial with an orange cap and a label with an orange border, which is authorized for use in individuals 5 through 11 years of age. The vial labels state: Age 5y to <12y. The carton labels state: For age 5 years to <12 years.

2 DOSAGE AND ADMINISTRATION

The storage, preparation, and administration information in this Prescribing Information apply to the Pfizer-BioNTech COVID-19 Vaccine, Bivalent which is supplied in multiple dose vials with orange caps and labels with orange borders.

Pfizer-BioNTech COVID-19 Vaccine, Bivalent Multiple Dose Vial with Orange Cap and a Label with an Orange Border

Age Range	Dilution Information	Doses Per Vial After Dilution	Dose Volume
5 through 11 years (Vial labels state: Age 5y to <12y)	Dilute with 1.3 mL sterile 0.9% Sodium Chloride Injection, USP prior to use	10	0.2 mL

2.1 Preparation for Administration

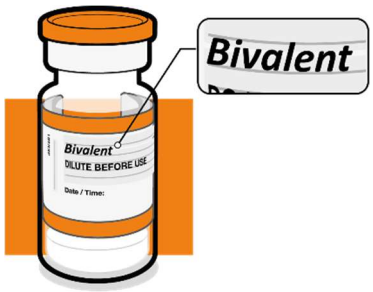
MUST BE DILUTED PRIOR TO USE.

Prior to Dilution

- The Pfizer-BioNTech COVID-19 Vaccine, Bivalent vials contain a frozen suspension that does not contain preservative. Each vial must be thawed before dilution.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)].
- Refer to thawing and preparation instructions in the panels below.

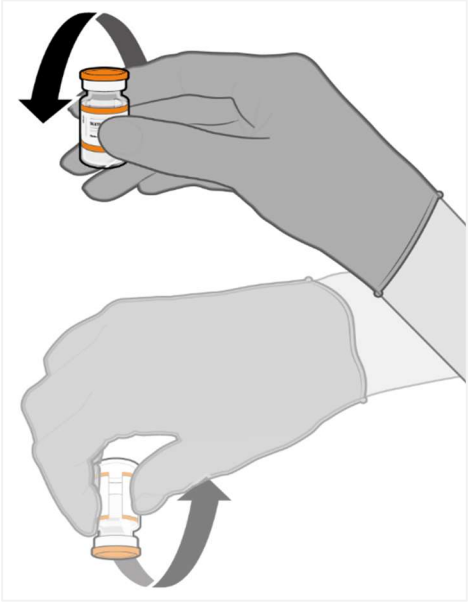
Dilution

- Dilute the vial contents using 1.3 mL of sterile 0.9% Sodium Chloride Injection, USP (not provided) to form the Pfizer-BioNTech COVID-19 Vaccine, Bivalent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. This diluent is not packaged with the vaccine and must be sourced separately. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent. Do not add more than 1.3 mL of diluent.
- After dilution, 1 vial contains 10 doses of 0.2 mL.

<table>
<tr><th colspan="2">Dilution and Preparation Instructions</th></tr>
<tr><td colspan="2">Pfizer-BioNTech COVID-19 Vaccine, Bivalent Vial with Orange Cap and Label with Orange Border – VIAL VERIFICATION</td></tr>
<tr><td> 

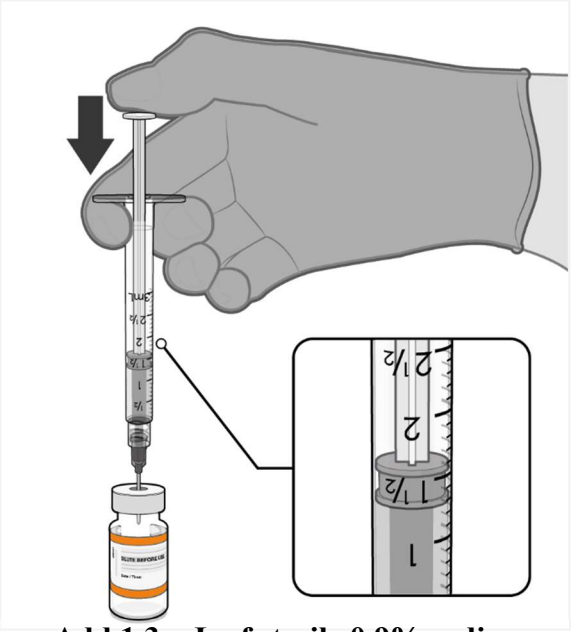
✓ Orange cap and label with orange border.</td><td>• Verify that the vial of Pfizer-BioNTech COVID-19 Vaccine, Bivalent:
○ has an orange cap and a label with an orange border,
○ states Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5), and
○ states “Age 5y to < 12y.”.</td></tr>
<tr><td colspan="2">THAWING PRIOR TO DILUTION</td></tr>
<tr><td> 

Store in the refrigerator for up to 10 weeks prior to use.</td><td>• Thaw vial(s) of Pfizer-BioNTech COVID-19 Vaccine, Bivalent before use either by:
○ Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)].
▪ A carton of 10 vials may take up to 4 hours to thaw.
○ Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes.
• Thawed vials can be stored in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 10 weeks prior to use.
• Thawed vials may be stored at room temperature [up to 25ºC (77ºF)] for up to 12 hours prior to use.</td></tr>
</table>

Dilution and Preparation Instructions	
 **Gently × 10**	• Before dilution, mix by inverting vaccine vial gently 10 times. • <u>Do not shake</u>. • 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.

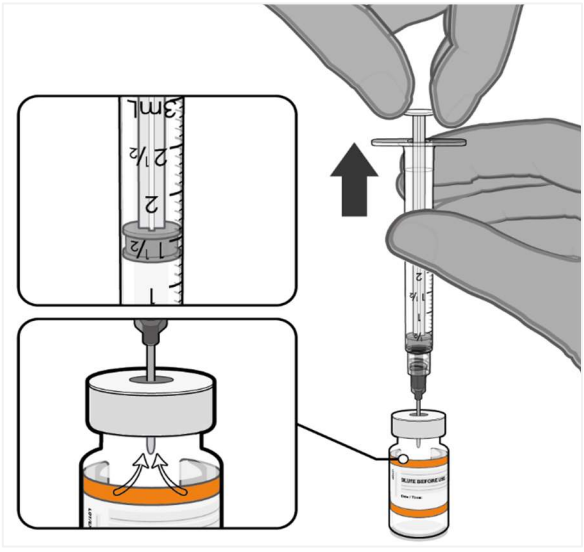
Dilution and Preparation Instructions

DILUTION



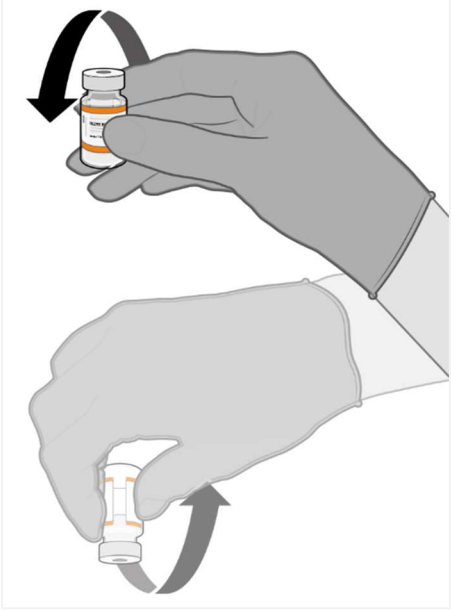
Add 1.3 mL of sterile 0.9% sodium chloride injection, USP.

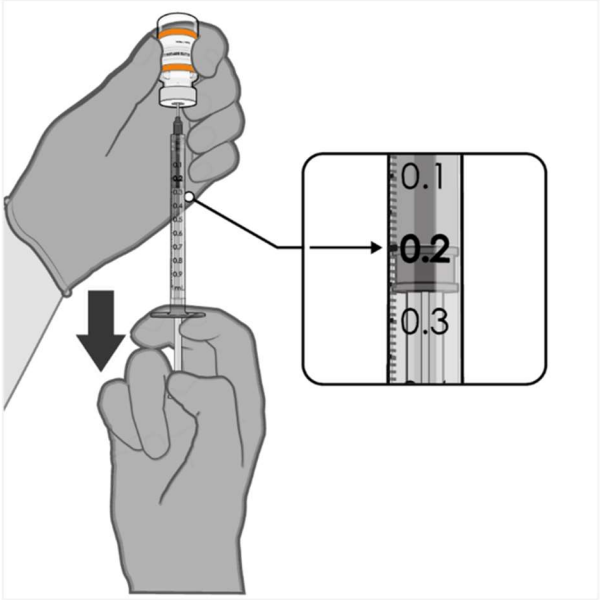
- Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent.
- Using aseptic technique, withdraw 1.3 mL of diluent into a transfer syringe (21-gauge or narrower needle).
- Cleanse the vaccine vial stopper with a single-use antiseptic swab.
- Add 1.3 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.



Pull back plunger to 1.3 mL to remove air from vial.

- Equalize vial pressure before removing the needle from the vial by withdrawing 1.3 mL air into the empty diluent syringe.

Dilution and Preparation Instructions	
 **Gently × 10**	• 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.** **Use within 12 hours after dilution.**	• Record the date and time of dilution on the Pfizer-BioNTech COVID-19 Vaccine, Bivalent vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 12 hours after dilution.

Dilution and Preparation Instructions	
WITHRAWAL OF INDIVIDUAL 0.2 mL DOSES	
 **Withdraw 0.2 mL dose of vaccine**	• 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. • Administer immediately. • 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.

2.2 Administration Information

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.

After withdrawing a single dose of 0.2 mL of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent, administer immediately.

2.3 Vaccination Schedule

A single booster dose (0.2 mL) of Pfizer-BioNTech COVID-19 Vaccine, Bivalent may be administered at least 2 months after completion of primary vaccination with any authorized or approved COVID-19 vaccine or after receipt of the most recent booster dose with any authorized monovalent COVID-19 vaccine.

3 DOSAGE FORMS AND STRENGTHS

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

Each dose of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent is 0.2 mL *[see Dosage and Administration (2.1)]*.

4 CONTRAINDICATIONS

Do not administer Pfizer-BioNTech COVID-19 Vaccine, Bivalent to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the Pfizer-BioNTech COVID-19 Vaccine or the Pfizer-BioNTech COVID-19 Vaccine, Bivalent *[see Description (13)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used 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 receipt of the second primary series dose or first booster dose, with most booster doses likely administered at least 5 months after completing primary vaccination. For the Pfizer-BioNTech COVID-19 Vaccine, the observed risk is higher among adolescent males and adult males under 40 years of age than among females and older males, and 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, in particular in adolescents. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Pfizer-BioNTech COVID-19 Vaccine, Bivalent.

5.5 Limitation of Effectiveness

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

6 OVERALL SAFETY SUMMARY

It is MANDATORY for vaccination providers to report to the Vaccine Adverse Event Reporting System (VAERS) 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 hospitalized or fatal cases of COVID-19 following vaccination with the Pfizer-BioNTech COVID-19 Vaccine, Bivalent.[4] To the extent feasible, provide a copy of the VAERS form to Pfizer Inc. Please see the REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS section for details on reporting to VAERS and Pfizer Inc.

The safety of a booster dose of Pfizer-BioNTech COVID-19 Vaccine, Bivalent is based on:

- safety data from a clinical study which evaluated a booster dose of Pfizer-BioNTech's bivalent COVID-19 vaccine (Original and Omicron BA.1), not authorized or approved, hereafter referred to as bivalent vaccine (Original and Omicron BA.1),
- safety data from clinical trials which evaluated primary and booster vaccination with Pfizer-BioNTech COVID-19 Vaccine, and
- postmarketing safety data with Pfizer-BioNTech COVID-19 Vaccine.

The safety data accrued with the bivalent vaccine (Original and Omicron BA.1) and with Pfizer-BioNTech COVID-19 Vaccine are relevant to Pfizer-BioNTech COVID-19 Vaccine, Bivalent because these vaccines are manufactured using the same process. The bivalent vaccine (Original and Omicron BA.1) contained 15 mcg of nucleoside-modified messenger RNA (modRNA) encoding the 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 lineage BA.1, for a total of 30 mcg modRNA per dose. This is the same total quantity of modRNA per dose as a dose of Pfizer-BioNTech COVID-19 Vaccine, Bivalent and as a dose of Pfizer-BioNTech COVID-19 Vaccine authorized for primary vaccination in individuals 12 years of age and older (and previously, but no longer, authorized for booster vaccination in individuals 12 years of age and older).

The clinical study that evaluated a booster dose of the bivalent vaccine (Original and Omicron BA.1) included participants greater than 55 years of age. Adverse reactions following administration of the bivalent vaccine (Original and Omicron BA.1) as a second booster dose included pain at the injection site (58.1%), fatigue (49.2%), headache (33.6%), muscle pain (22.3%), chills (13.0%), joint pain (11.3%), injection site redness (7.0%), injection site swelling (6.6%), fever (5.0%), lymphadenopathy (0.3%), nausea (0.3%), and malaise (0.3%).

In a clinical study in participants 5 through 11 years of age, adverse reactions following administration of a single booster dose of Pfizer-BioNTech COVID-19 Vaccine were injection site pain (73.9%), fatigue (45.6%), headache (34.0%), muscle pain (18.3%), injection site swelling (16.4%), injection site redness (15.6%), chills (10.5%), fever (6.7%), joint pain (6.7%), diarrhea (4.9%), lymphadenopathy (2.5%), and vomiting (2.4%).

Post Authorization Experience

Severe allergic reactions, including anaphylaxis, have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine.

Myocarditis and pericarditis have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine.

[4] Vaccination providers administering COMIRNATY (COVID-19 Vaccine, mRNA) and Pfizer-BioNTech COVID-19 Vaccine must adhere to the same reporting requirements.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Overall 3,013 participants 6 months through 4 years of age and 3,109 participants 5 through 11 years of age in Study 3 (NCT04816643) and 22,851 participants 12 years of age and older in Study 1 (NCT04380701) and Study 2 (NCT04368728) have received at least 1 dose of Pfizer-BioNTech COVID-19 Vaccine during the Phase 2/3 blinded placebo-controlled follow-up period. In a subset of Study 4 (NCT04955626), 305 participants greater than 55 years of age received a second booster dose with the 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

Table 1 and Table 2 present the frequency and severity of reported solicited local reactions and systemic reactions, respectively, within 7 days of a second booster dose of Pfizer-BioNTech COVID-19 Vaccine or bivalent vaccine (Original and Omicron BA.1).

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 1: 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 2: 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
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)

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

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).

Pfizer-BioNTech COVID-19 Vaccine

Primary Series

The safety of the primary series Pfizer-BioNTech COVID-19 Vaccine was evaluated in participants 5 years 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 or 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 3109 participants received Pfizer-BioNTech COVID-19 Vaccine (10 mcg modRNA) and 1538 participants received placebo in Phase 2/3.

In Study 2 and Study 3, all participants 5 through 11 years of age, 12 through 15 years of age, and 16 years of age and older in the reactogenicity subset, 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 (all unsolicited adverse events) after the last vaccination or 6 months (serious adverse events) after the last vaccination]. Tables 1 and 2 present the frequency and severity of solicited local and systemic reactions, respectively, within 7 days following each dose of Pfizer-BioNTech COVID 19 Vaccine (10 mcg modRNA) and placebo in participants 5 through 11 years of age.

Participants 5 Through 11 Years of Age

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.

Unsolicited Adverse Events

In the following analyses of Study 3 in participants 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 – 3.7 weeks), non-serious adverse events from Dose 1 through the cutoff date of October 8, 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 6 Through 23 Months of Age

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.

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.

Participants 2 Through 4 Years of Age

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] were 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.

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 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 12 Through 15 Years of Age

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.

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 16 Years of Age and Older

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 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.

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. 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.

First Booster Dose Following a Primary Series of Pfizer-BioNTech COVID-19 Vaccine 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 the 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 3 and Table 4 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 3: 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.

	Pfizer-BioNTech COVID-19 Vaccine± Booster Na=371 nb (%)

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 4: 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 Na=371 nb (%)
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)

Solicited Systemic Reaction	Pfizer-BioNTech COVID-19 Vaccine± Booster Na=371 nb (%)
New or worsened muscle pain[c]	
Any	68 (18.3)
Mild	40 (10.8)
Moderate	28 (7.5)
Severe	0
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 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 the 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 booster dose through the cutoff date.

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.

Unsolicited Adverse Events

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

In an analysis of all unsolicited adverse events reported following the 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 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 Primary 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.

Second Booster Dose Following Primary Series and First Booster Vaccination

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.

6.2 Post Authorization Experience

The following adverse reactions have been identified during post authorization use of Pfizer-BioNTech COVID-19 Vaccine. 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

8 REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS[5]

See Overall Safety Summary (Section 6) for additional information.

The vaccination provider enrolled in the federal COVID-19 Vaccination Program is responsible for MANDATORY reporting of the listed events following administration of 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 children and adults
- Cases of COVID-19 that result 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 1 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 1 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.

[5] Vaccination providers administering COMIRNATY (COVID-19 Vaccine, mRNA) or Pfizer-BioNTech COVID-19 Vaccine must adhere to the same reporting requirements.

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 the 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 1 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

10 DRUG INTERACTIONS

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

11 USE IN SPECIFIC POPULATIONS

11.1 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 US 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 (mRNA) (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.

11.2 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.

11.3 Pediatric Use

Emergency Use Authorization of Pfizer-BioNTech COVID-19 Vaccine, Bivalent for use as a booster dose in individuals 5 through 17 years of age is based on the safety and effectiveness data of Pfizer-BioNTech COVID-19 Vaccine in individuals 6 months of age and older and safety and immunogenicity data with the bivalent vaccine (Original and Omicron BA.1) in individuals greater than 55 years of age.

Pfizer-BioNTech COVID-19 Vaccine, Bivalent is not authorized for use in individuals younger than 5 years of age as a booster dose.

13 DESCRIPTION

The Pfizer-BioNTech COVID-19 Vaccine, Bivalent is supplied as a sterile, frozen suspension in multiple dose vials with orange caps and labels with orange borders; 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 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 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.

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

14 CLINICAL PHARMACOLOGY

14.1 Mechanism of Action

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.

18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA

The effectiveness of a booster dose of Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5) is based on effectiveness of primary and booster vaccination with Pfizer-BioNTech COVID-19 Vaccine and immunogenicity of a second booster dose with the bivalent vaccine (Original and Omicron BA.1).

18.1 Efficacy of 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 5 presents the specific demographic characteristics in the studied population.

Table 5: 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 multiracial 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 6.

Table 6: 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.

18.2 Efficacy of 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 7 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 7: 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)

	Pfizer-BioNTech COVID-19 Vaccine* 10 mcg/Dose (N[a]=1305) n[b] (%)	Placebo (N[a]=663) n[b] (%)
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 8. 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 8: 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.

18.3 Immunogenicity of 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 9 and Table 10).

Table 9: 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 10: 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.

18.4 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 50% neutralizing titer (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 11).

Noninferiority 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 12). A descriptive summary of seroresponse to the Original strain is also included in Table 12.

Table 11: 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 12: 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).

18.5 Immunogenicity of a First Booster Dose With a 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]).

18.6 Immunogenicity of a First Booster Dose Following a 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.

19 HOW SUPPLIED/STORAGE AND HANDLING

Pfizer-BioNTech COVID-19 Vaccine, Bivalent is a suspension for intramuscular injection. Multiple dose vials with orange caps and labels with orange borders are supplied in a carton containing 10 multiple dose vials. After dilution, 1 vial contains 10 doses of 0.2 mL.

- Carton of 10 multiple dose vials: NDC 59267-0565-2
- Multiple dose vial: NDC 59267-0565-1

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. A carton of 10 vials may take up to 4 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 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 dilution. After dilution, the vial should be held between 2°C to 25°C (35°F to 77°F). Vials should be discarded 12 hours after dilution.

Transportation of Vials

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

20 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.

21 CONTACT 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

Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1542-2.3c

Revised: 8 December 22