ENGLISH

FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE (VACCINATION PROVIDERS)

EMERGENCY USE AUTHORIZATION (EUA) OF THE PFIZER-BIONTECH COVID-19 VACCINE TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19)

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, for active immunization to prevent COVID-19 in individuals 12 years of age and older and to provide a third dose to individuals 12 years of age and older who have been determined to have certain kinds of immunocompromise.

COMIRNATY (COVID-19 Vaccine, mRNA) is an FDA-approved COVID-19 vaccine made by Pfizer for BioNTech. It is approved as a 2-dose series for the prevention of COVID-19 in individuals 16 years of age and older and is also authorized for emergency use in individuals 12 through 15 years and to provide a third dose to individuals 12 years of age and older who have been determined to have certain kinds of immunocompromise.

The FDA-approved COMIRNATY (COVID-19 Vaccine, mRNA) and the EUA-authorized Pfizer-BioNTech COVID-19 Vaccine have the same formulation and can be used interchangeably to provide the COVID-19 vaccination series.[1]

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 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. See “MANDATORY REQUIREMENTS FOR PFIZER-BIONTECH COVID-19 VACCINE ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION” for reporting requirements.

The Pfizer-BioNTech COVID-19 Vaccine is a suspension for intramuscular injection administered as a series of two doses (0.3 mL each) 3 weeks apart.

A third dose of the Pfizer-BioNTech COVID-19 Vaccine (0.3 mL) administered at least 28 days following the second dose of this vaccine is authorized for administration to individuals at least 12 years of age who have undergone solid

[1] The licensed vaccine has the same formulation as the EUA-authorized vaccine and the products can be used interchangeably to provide the vaccination series without presenting any safety or effectiveness concerns. The products are legally distinct with certain differences that do not impact safety or effectiveness.

organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

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 for active immunization against 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.

DOSAGE AND ADMINISTRATION

Storage and Handling

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

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of Pfizer-BioNTech COVID-19 Vaccine Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. This information in the package insert supersedes the storage conditions printed on the vial cartons.

Cartons and vials of Pfizer-BioNTech COVID-19 Vaccine with an expiry date of August 2021 through February 2022 printed on the label may remain in use for 3 months beyond the printed date as long as approved storage conditions between -90ºC to -60ºC (-130ºF to -76ºF) have been maintained. Updated expiry dates are shown below.

Printed Expiry Date		Updated Expiry Date
August 2021	→	November 2021
September 2021	→	December 2021
October 2021	→	January 2022
November 2021	→	February 2022
December 2021	→	March 2022
January 2022	→	April 2022
February 2022	→	May 2022

If not stored between -90ºC to -60ºC (-130ºF to -76ºF), vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned one time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which the Pfizer-BioNTech COVID-19 Vaccine arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned one time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration
Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature
For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions. Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of one or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

- After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution.
- During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.
- Any vaccine remaining in vials must be discarded after 6 hours.
- Do not refreeze.

Dosing and Schedule

The Pfizer-BioNTech COVID-19 Vaccine is administered intramuscularly as a series of two doses (0.3 mL each) 3 weeks apart.

The FDA-approved COMIRNATY (COVID-19 Vaccine, mRNA) and the EUA-authorized Pfizer-BioNTech COVID-19 Vaccine have the same formulation and can be used interchangeably to provide the COVID-19 vaccination series.[2]

There are no data available on the interchangeability of the Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY (COVID-19 Vaccine, mRNA) with other COVID-19 vaccines to complete the vaccination series.

A third dose of the Pfizer-BioNTech COVID-19 vaccine (0.3 mL) administered at least 28 days following the second dose of this vaccine is authorized for administration to individuals at least 12 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

Dose Preparation

Prior to Dilution

- The Pfizer-BioNTech COVID-19 Vaccine Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *(see Storage and Handling)*.

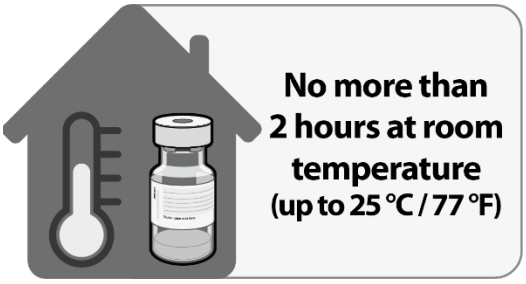
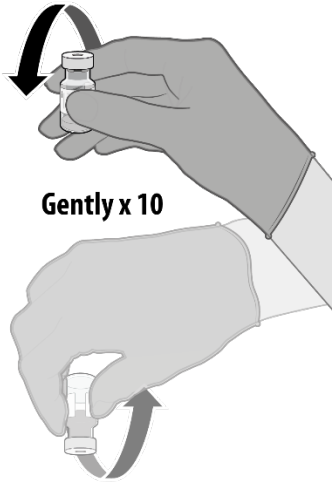
[2] The licensed vaccine has the same formulation as the EUA-authorized vaccine and the products can be used interchangeably to provide the vaccination series without presenting any safety or effectiveness concerns. The products are legally distinct with certain differences that do not impact safety or effectiveness.

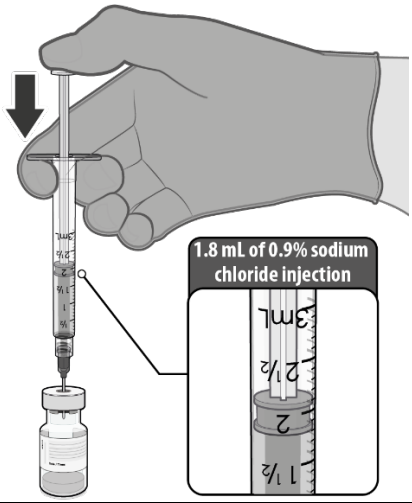
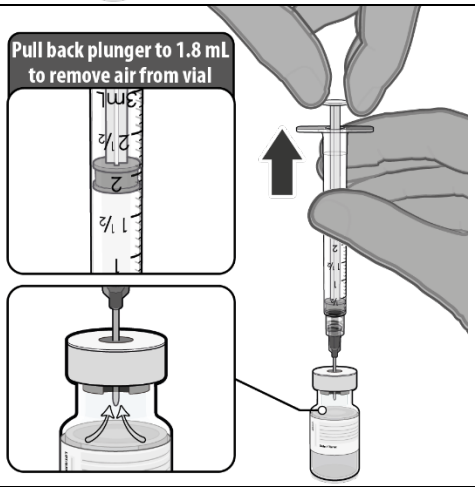
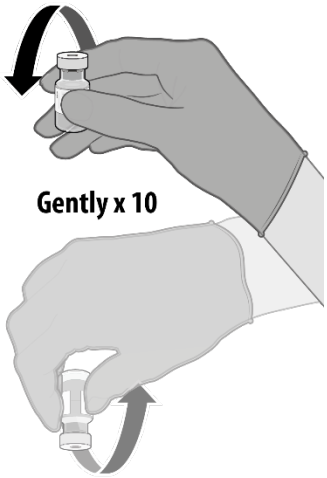
- Refer to thawing instructions in the panels below.

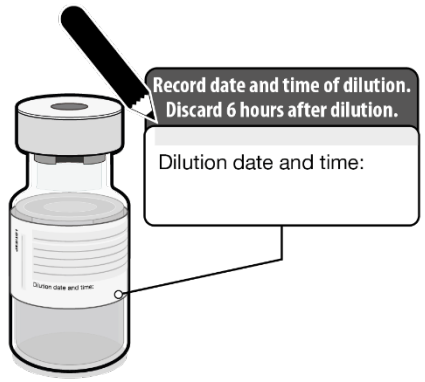
Dilution
Dilute the vial contents using 1.8 mL of 0.9% Sodium Chloride Injection, USP (not provided) to form the Pfizer-BioNTech COVID-19 Vaccine. ONLY use 0.9% Sodium Chloride Injection, USP as the diluent. This diluent is not packaged with the vaccine and must be sourced separately. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent. Do not add more than 1.8 mL of diluent.

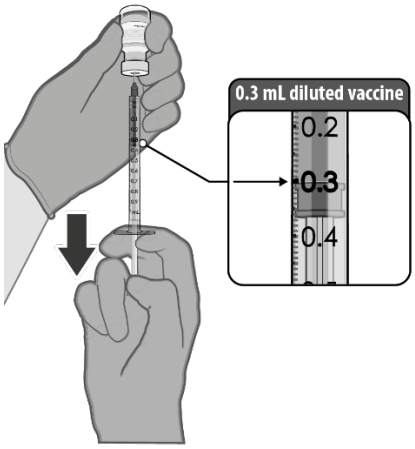
After dilution, one vial contains 6 doses of 0.3 mL. Vial labels and cartons may state that after dilution, a vial contains 5 doses of 0.3 mL. The information in this Fact Sheet regarding the number of doses per vial after dilution supersedes the number of doses stated on vial labels and cartons.

- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	
	• Thaw vial(s) of Pfizer-BioNTech COVID-19 Vaccine before use either by: ○ Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. ○ Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
	• Before dilution invert vaccine vial gently 10 times. • Do not shake. • Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.

DILUTION	
	• Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent. • Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Cleanse the vaccine vial stopper with a single-use antiseptic swab. • Add 1.8 mL of 0.9% Sodium Chloride Injection, USP into the vaccine vial.
	• Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing the Pfizer-BioNTech COVID-19 Vaccine 10 times to mix. • <u>Do not shake</u>. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.

	• Record the date and time of dilution on the Pfizer-BioNTech COVID-19 Vaccine vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF PFIZER-BIONTECH COVID-19 VACCINE	
	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of the Pfizer-BioNTech COVID-19 Vaccine preferentially using a low dead-volume syringe and/or needle. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

Administration

Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

Administer the Pfizer-BioNTech COVID-19 Vaccine intramuscularly.

After dilution, vials of Pfizer-BioNTech COVID-19 Vaccine contain six doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract six doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle:

- Each dose must contain 0.3 mL of vaccine.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and content.
- Do not pool excess vaccine from multiple vials.

Contraindications

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

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

Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. 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.

Limitation of Effectiveness

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

Adverse Reactions

Adverse Reactions in Clinical Trials
Adverse reactions following the Pfizer-BioNTech COVID-19 Vaccine that have been reported in clinical trials include injection site pain, fatigue, headache, muscle pain, chills, joint pain, fever, injection site swelling, injection site redness, nausea, malaise, and lymphadenopathy *(see Full EUA Prescribing Information)*.

Adverse Reactions in Post Authorization Experience
Severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema), diarrhea, vomiting, and pain in extremity (arm) have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine outside of clinical trials.

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

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

Use with Other Vaccines

There is no information on the co-administration of the Pfizer-BioNTech COVID-19 Vaccine 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 “Vaccine Information Fact Sheet for Recipients and Caregivers” (and provide a copy or direct the individual to the website www.cvdvaccine.com to obtain the Vaccine Information Fact Sheet) prior to the individual receiving each dose of Pfizer-BioNTech COVID-19 Vaccine, including:

- FDA has authorized the emergency use of the Pfizer-BioNTech COVID-19 Vaccine, which is not an FDA-approved vaccine.
- The recipient or their caregiver has the option to accept or refuse Pfizer-BioNTech COVID-19 Vaccine.

- The significant known and potential risks and benefits of Pfizer-BioNTech COVID-19 Vaccine, 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 to prevent COVID-19, please see www.clinicaltrials.gov.

Provide a vaccination card to the recipient or their caregiver with the date when the recipient needs to return for the second dose of Pfizer-BioNTech COVID-19 Vaccine.

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 second-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 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, the following items are required. Use of unapproved Pfizer-BioNTech COVID-19 Vaccine 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 is authorized for use in individuals 12 years of age and older.

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

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

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

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 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 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 MIS in adults and children, and cases of COVID-19 that result in hospitalization or death following administration of Pfizer-BioNTech COVID-19 Vaccine to recipients.

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

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 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

COMIRNATY (COVID-19 Vaccine, mRNA) is an FDA-approved COVID-19 vaccine made by Pfizer for BioNTech. It is approved as a 2-dose series for use in individuals 16 years of age and older. COMIRNATY (COVID-19 Vaccine, mRNA) is also authorized for emergency use in individuals 12 through 15 years of age and to provide a third dose to individuals 12 years of age and older who have been determined to have certain kinds of immunocompromise. COMIRNATY (COVID-19 Vaccine, mRNA) has the same formulation as the Pfizer-BioNTech COVID-19 Vaccine. These vaccines can be used interchangeably to provide the COVID-19 vaccination series.[4]

There may be clinical trials or availability under EUA of other COVID-19 vaccines.

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

[4] The licensed vaccine has the same formulation as the EUA-authorized vaccine and the products can be used interchangeably to provide the vaccination series without presenting any safety or effectiveness concerns. The products are legally distinct with certain differences that do not impact safety or effectiveness.

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, for active immunization against COVID-19 in individuals 12 years of age and older and to provide a third dose to individuals 12 years of age and older who have been determined to have certain kinds of immunocompromise. FDA-approved COMIRNATY is also authorized in individuals 12 through 15 years and to provide a third dose to individuals 12 years of age and older who have been determined to have certain kinds of immunocompromise.

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 and COMIRNATY 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 and COMIRNATY 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 used to prevent COVID-19, visit www.hrsa.gov/cicp, email cicp@hrsa.gov, or call: 1-855-266-2427.

Manufactured by
Pfizer Inc., New York, NY 10017

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

LAB-1450-11.4

Revised: 23 August 2021

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

FULL EMERGENCY USE AUTHORIZATION PRESCRIBING INFORMATION: CONTENTS*

1 AUTHORIZED USE
2 DOSAGE AND ADMINISTRATION
2.1 Preparation for Administration
2.2 Administration Information
2.3 Vaccination Schedule for Individuals 12 Years of Age and Older
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Management of Acute Allergic Reactions
5.2 Myocarditis and Pericarditis
5.3 Syncope
5.4 Altered Immunocompetence
5.5 Limitation of Effectiveness
6 OVERALL SAFETY SUMMARY
6.1 Clinical Trials Experience
6.2 Post Authorization Experience
8 REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS
10 DRUG INTERACTIONS
11 USE IN SPECIFIC POPULATIONS
11.1 Pregnancy
11.2 Lactation
11.3 Pediatric Use
11.4 Geriatric Use
11.5 Use in Immunocompromised
13 DESCRIPTION
14 CLINICAL PHARMACOLOGY
14.1 Mechanism of Action
18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA
18.1 Efficacy in Participants 16 Years of Age and Older
18.2 Efficacy in Adolescents 12 Through 15 Years of Age
18.3 Immunogenicity in Adolescents 12 Through 15 Years of Age
18.4 Immunogenicity in Solid Organ Transplant Recipients
19 HOW SUPPLIED/STORAGE AND HANDLING
20 PATIENT COUNSELING INFORMATION
21 CONTACT INFORMATION

* 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 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 12 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Preparation for Administration

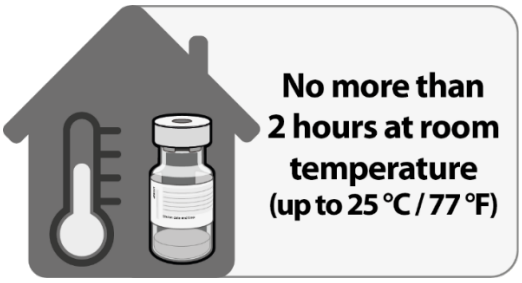
Prior to Dilution

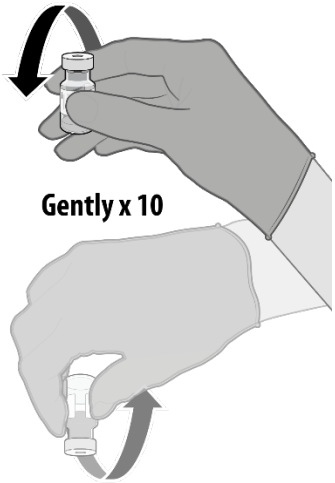
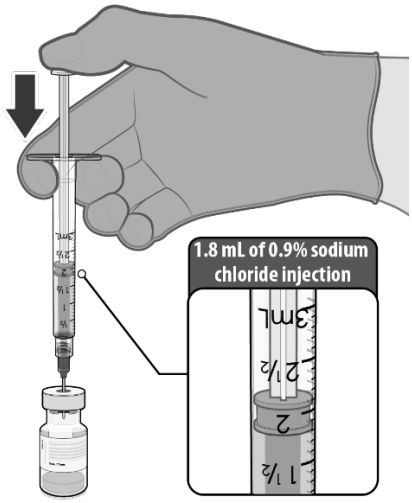
- The Pfizer-BioNTech COVID-19 Vaccine Multiple Dose Vial contains a volume of 0.45 mL, supplied as a frozen suspension that does not contain preservative. Each vial must be thawed and diluted prior to administration.
- Vials may be thawed in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] or at room temperature [up to 25ºC (77ºF)] *[see How Supplied/Storage and Handling (19)]*.
- Refer to thawing instructions in the panels below.

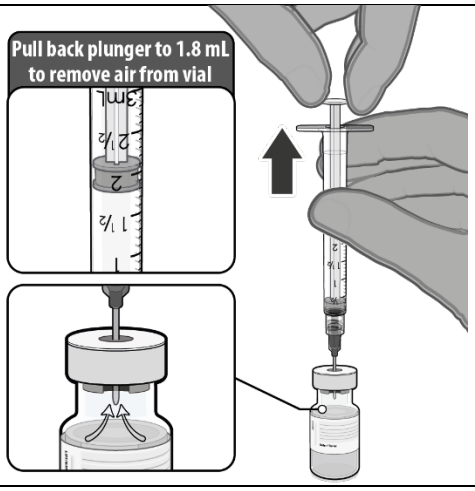
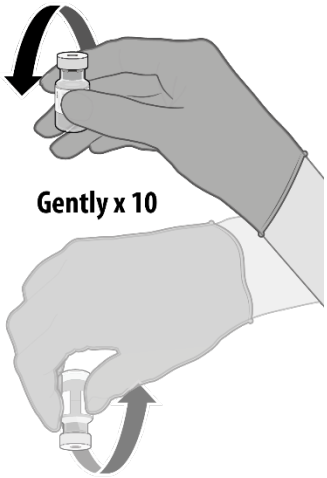
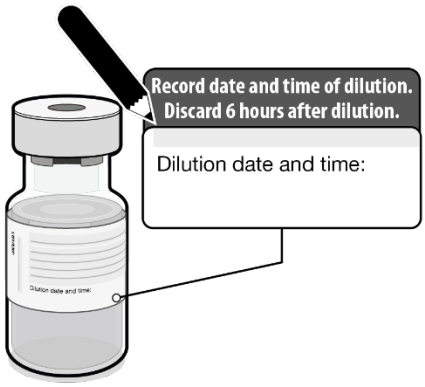
Dilution

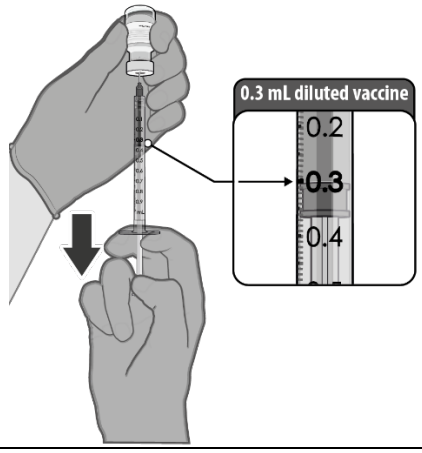
- Dilute the vial contents using 1.8 mL of 0.9% Sodium Chloride Injection, USP (not provided) to form the Pfizer-BioNTech COVID-19 Vaccine. Do not add more than 1.8 mL of diluent.
- ONLY use 0.9% Sodium Chloride Injection, USP as the diluent. This diluent is not packaged with the vaccine and must be sourced separately. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- After dilution, one vial contains 6 doses of 0.3 mL. Vial labels and cartons may state that after dilution, a vial contains 5 doses of 0.3 mL. The information in this Full EUA Prescribing Information regarding the number of doses per vial after dilution supersedes the number of doses stated on vial labels and cartons.
- Refer to dilution and dose preparation instructions in the panels below.

THAWING PRIOR TO DILUTION	

	• Thaw vial(s) of Pfizer-BioNTech COVID-19 Vaccine before use either by:
	  o Allowing vial(s) to thaw in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month.
	  o Allowing vial(s) to sit at room temperature [up to 25ºC (77ºF)] for 30 minutes.
	• Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.

	• Before dilution invert 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 <u>white to off-white opaque amorphous particles</u>. • Do not use if liquid is discolored or if other particles are observed.
DILUTION	
	• Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent. • Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle). • Cleanse the vaccine vial stopper with a single-use antiseptic swab. • Add 1.8 mL of 0.9% Sodium Chloride Injection, USP into the vaccine vial.

	• Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.
	• Gently invert the vial containing the Pfizer-BioNTech COVID-19 Vaccine 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
	• Record the date and time of dilution on the Pfizer-BioNTech COVID-19 Vaccine vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF PFIZER-BIONTECH COVID-19 VACCINE	
	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of the Pfizer-BioNTech COVID-19 Vaccine preferentially using low dead-volume syringes and/or needles. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

2.2 Administration Information

Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

Administer the Pfizer-BioNTech COVID-19 Vaccine intramuscularly.

After dilution, vials of Pfizer-BioNTech COVID-19 Vaccine contain six doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract six doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. Irrespective of the type of syringe and needle:

- Each dose must contain 0.3 mL of vaccine.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- Do not pool excess vaccine from multiple vials.

2.3 Vaccination Schedule for Individuals 12 Years of Age and Older

The Pfizer-BioNTech COVID-19 Vaccine is administered intramuscularly as a series of two doses (0.3 mL each) three weeks apart.

The FDA-approved COMIRNATY (COVID-19 Vaccine, mRNA) and the EUA-authorized Pfizer-BioNTech COVID-19 Vaccine have the same formulation and can be used interchangeably to provide the COVID-19 vaccination series.[5] There are no data available on the interchangeability of the Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY (COVID-19 Vaccine, mRNA) with other COVID-19 vaccines to complete the vaccination series. Individuals who have received one dose of Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY (COVID-19 Vaccine, mRNA should receive a second dose of Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY (COVID-19 Vaccine, mRNA) to complete the vaccination series.

[5] The licensed vaccine has the same formulation as the EUA-authorized vaccine and the products can be used interchangeably to provide the vaccination series without presenting any safety or effectiveness concerns. The products are legally distinct with certain differences that do not impact safety or effectiveness.

A third dose of the Pfizer-BioNTech COVID-19 vaccine (0.3 mL) administered at least 28 days following the second dose of this vaccine is authorized for administration to individuals at least 12 years of age who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

3 DOSAGE FORMS AND STRENGTHS

Pfizer-BioNTech COVID-19 Vaccine is a suspension for injection. After preparation, a single dose is 0.3 mL.

4 CONTRAINDICATIONS

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

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

5.2 Myocarditis and Pericarditis

Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. 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.

5.5 Limitation of Effectiveness

The Pfizer-BioNTech COVID-19 Vaccine 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 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. [6] 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.

In clinical studies, adverse reactions in participants 16 years of age and older included pain at the injection site (84.1%), fatigue (62.9%), headache (55.1%), muscle pain (38.3%), chills (31.9%), joint pain (23.6%), fever (14.2%), injection site swelling (10.5%), injection site redness (9.5%), nausea (1.1%), malaise (0.5%), and lymphadenopathy (0.3%).

In a clinical study, adverse reactions in adolescents 12 through 15 years of age included pain at the injection site (90.5%), fatigue (77.5%), headache (75.5%), chills (49.2%), muscle pain (42.2%), fever (24.3%), joint pain (20.2%), injection site swelling (9.2%), injection site redness (8.6%), lymphadenopathy (0.8%), and nausea (0.4%).

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

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

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.

The safety of Pfizer-BioNTech COVID-19 Vaccine was evaluated in participants 12 years of age and older in two clinical studies conducted in the United States, Europe, Turkey, South Africa, and South America. Study BNT162-01 (Study 1) was a Phase 1/2, two-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; 21,728 placebo) in Phase 2/3 are 16 years of age or older (including 138 and 145 adolescents 16 and 17 years of age in the vaccine and placebo groups, respectively) and 2,260 adolescents are 12 through 15 years of age (1,131 and 1,129 in the vaccine and placebo groups, respectively).

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

In Study 2, all participants 12 to <16 years of age, and participants 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) or 6 months (serious adverse events) after the last vaccination]. Tables 1 through 6 present the frequency and severity of solicited local and systemic reactions, respectively, within 7 days following each dose of Pfizer-BioNTech COVID 19 Vaccine and placebo.

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 and 18,785 placebo) participants 16 years of age or older had been followed for a median of 2 months after the second dose of Pfizer-BioNTech COVID-19 Vaccine.

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.

Solicited Local and Systemic Adverse Reactions

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

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

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

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

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

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

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

	Pfizer-BioNTech COVID-19 Vaccine Dose 1 N[a]=2291 n[b] (%)	Placebo Dose 1 N[a]=2298 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N[a]=2098 n[b] (%)	Placebo Dose 2 N[a]=2103 n[b] (%)
Fever				
≥38.0°C	85 (3.7)	20 (0.9)	331 (15.8)	10 (0.5)
≥38.0°C to 38.4°C	64 (2.8)	10 (0.4)	194 (9.2)	5 (0.2)
>38.4°C to 38.9°C	15 (0.7)	5 (0.2)	110 (5.2)	3 (0.1)
>38.9°C to 40.0°C	6 (0.3)	3 (0.1)	26 (1.2)	2 (0.1)
>40.0°C	0 (0.0)	2 (0.1)	1 (0.0)	0 (0.0)
Fatigue[c]				
Any	1085 (47.4)	767 (33.4)	1247 (59.4)	479 (22.8)
Mild	597 (26.1)	467 (20.3)	442 (21.1)	248 (11.8)
Moderate	455 (19.9)	289 (12.6)	708 (33.7)	217 (10.3)
Severe	33 (1.4)	11 (0.5)	97 (4.6)	14 (0.7)
Headache[c]				
Any	959 (41.9)	775 (33.7)	1085 (51.7)	506 (24.1)
Mild	628 (27.4)	505 (22.0)	538 (25.6)	321 (15.3)
Moderate	308 (13.4)	251 (10.9)	480 (22.9)	170 (8.1)
Severe	23 (1.0)	19 (0.8)	67 (3.2)	15 (0.7)
Chills[c]				
Any	321 (14.0)	146 (6.4)	737 (35.1)	79 (3.8)
Mild	230 (10.0)	111 (4.8)	359 (17.1)	65 (3.1)
Moderate	82 (3.6)	33 (1.4)	333 (15.9)	14 (0.7)
Severe	9 (0.4)	2 (0.1)	45 (2.1)	0 (0.0)

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

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

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

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

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

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

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

	Pfizer-BioNTech COVID-19 Vaccine Dose 1 N[a]=1802 n[b] (%)	Placebo Dose 1 N[a]=1792 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N[a]=1660 n[b] (%)	Placebo Dose 2 N[a]=1646 n[b] (%)
Fever				
≥38.0°C	26 (1.4)	7 (0.4)	181 (10.9)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.3)	2 (0.1)	131 (7.9)	2 (0.1)
>38.4°C to 38.9°C	1 (0.1)	3 (0.2)	45 (2.7)	1 (0.1)
>38.9°C to 40.0°C	1 (0.1)	2 (0.1)	5 (0.3)	1 (0.1)
>40.0°C	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue[c]				
Any	615 (34.1)	405 (22.6)	839 (50.5)	277 (16.8)
Mild	373 (20.7)	252 (14.1)	351 (21.1)	161 (9.8)
Moderate	240 (13.3)	150 (8.4)	442 (26.6)	114 (6.9)
Severe	2 (0.1)	3 (0.2)	46 (2.8)	2 (0.1)

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

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

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

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, in 99 individuals who had undergone various solid

organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported in recipients who were followed for one month following post Dose 3.

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 7960 participants 56 years of age and older received Pfizer-BioNTech COVID-19 Vaccine, non-serious adverse events within 30 days were reported in 23.8% of participants who received Pfizer-BioNTech COVID-19 Vaccine and 11.7% of participants in the placebo group, for participants who received at least 1 dose. In these analyses, 91.6% of study participants had at least 30 days of follow-up after Dose 2.

The higher frequency of reported unsolicited non-serious adverse events among Pfizer-BioNTech COVID-19 Vaccine recipients compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following vaccination that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Tables 3 and 4. From Dose 1 through 30 days after Dose 2, reports of lymphadenopathy were imbalanced with notably more cases in the Pfizer-BioNTech COVID-19 Vaccine group (64) vs. the placebo group (6), which is plausibly related to vaccination. Throughout the safety follow-up period to date, Bell's palsy (facial paralysis) was reported by four 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.

Adolescents 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 adolescents (1,131 Pfizer-BioNTech COVID-19 Vaccine; 1,129 placebo) were 12 through 15 years of age. Of these, 1,308 (660 Pfizer-BioNTech COVID-19 Vaccine and 648 placebo) adolescents have been followed for at least 2 months after the second dose of Pfizer-BioNTech COVID-19 Vaccine. 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 adolescents who received Pfizer-BioNTech COVID-19 Vaccine and those who received placebo. Overall, among the adolescents who received the Pfizer-BioNTech COVID-19 Vaccine, 50.1% were male and 49.9% were female, 85.9% were White, 4.6% were Black or African American, 11.7% were Hispanic/Latino, 6.4% were Asian, and 0.4% were American Indian/Alaska Native.

Solicited Local and Systemic Adverse Reactions

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

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

	Pfizer-BioNTech COVID-19 Vaccine Dose 1 N[a]=1127 n[b] (%)	**Placebo Dose 1 N[a]=1127 n[b] (%)**	**Pfizer-BioNTech COVID-19 Vaccine Dose 2 N[a]=1097 n[b] (%)**	**Placebo Dose 2 N[a]=1078 n[b] (%)**
Redness[c]				
Any (>2 cm)	65 (5.8)	12 (1.1)	55 (5.0)	10 (0.9)
Mild	44 (3.9)	11 (1.0)	29 (2.6)	8 (0.7)
Moderate	20 (1.8)	1 (0.1)	26 (2.4)	2 (0.2)
Severe	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Swelling[c]				
Any (>2 cm)	78 (6.9)	11 (1.0)	54 (4.9)	6 (0.6)
Mild	55 (4.9)	9 (0.8)	36 (3.3)	4 (0.4)
Moderate	23 (2.0)	2 (0.2)	18 (1.6)	2 (0.2)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

	Pfizer-BioNTech COVID-19 Vaccine Dose 1 N[a]=1127 n[b] (%)	Placebo Dose 1 N[a]=1127 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N[a]=1097 n[b] (%)	Placebo Dose 2 N[a]=1078 n[b] (%)
Pain at the injection site[d]				
Any	971 (86.2)	263 (23.3)	866 (78.9)	193 (17.9)
Mild	467 (41.4)	227 (20.1)	466 (42.5)	164 (15.2)
Moderate	493 (43.7)	36 (3.2)	393 (35.8)	29 (2.7)
Severe	11 (1.0)	0 (0.0)	7 (0.6)	0 (0.0)

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

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

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

	Pfizer-BioNTech COVID-19 Vaccine Dose 1 N[a]=1127 n[b] (%)	Placebo Dose 1 N[a]=1127 n[b] (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N[a]=1097 n[b] (%)	Placebo Dose 2 N[a]=1078 n[b] (%)
Vomiting[d]				
Any	31 (2.8)	10 (0.9)	29 (2.6)	12 (1.1)
Mild	30 (2.7)	8 (0.7)	25 (2.3)	11 (1.0)
Moderate	0 (0.0)	2 (0.2)	4 (0.4)	1 (0.1)
Severe	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Diarrhea[e]				
Any	90 (8.0)	82 (7.3)	65 (5.9)	43 (4.0)
Mild	77 (6.8)	72 (6.4)	59 (5.4)	38 (3.5)
Moderate	13 (1.2)	10 (0.9)	6 (0.5)	5 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
New or worsened muscle pain[c]				
Any	272 (24.1)	148 (13.1)	355 (32.4)	90 (8.3)
Mild	125 (11.1)	88 (7.8)	152 (13.9)	51 (4.7)
Moderate	145 (12.9)	60 (5.3)	197 (18.0)	37 (3.4)
Severe	2 (0.2)	0 (0.0)	6 (0.5)	2 (0.2)
New or worsened joint pain[c]				
Any	109 (9.7)	77 (6.8)	173 (15.8)	51 (4.7)
Mild	66 (5.9)	50 (4.4)	91 (8.3)	30 (2.8)
Moderate	42 (3.7)	27 (2.4)	78 (7.1)	21 (1.9)
Severe	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)
Use of antipyretic or pain medication[f]	413 (36.6)	111 (9.8)	557 (50.8)	95 (8.8)

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

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

Unsolicited Adverse Events

In the following analyses of Study 2 in adolescents 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.

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)

8 REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS[7]

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 Pfizer-BioNTech COVID-19 Vaccine 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 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 one of the outcomes listed above

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

Instructions for Reporting to VAERS

The vaccination provider enrolled in the federal COVID-19 Vaccination Program should complete and submit a VAERS form to FDA using one of the following methods:

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

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

- Patient demographics (e.g., patient name, date of birth)
- Pertinent medical history
- Pertinent details regarding admission and course of illness
- Concomitant medications
- Timing of adverse event(s) in relationship to administration of the Pfizer-BioNTech COVID-19 Vaccine
- 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 and any other vaccines administered on the same day; and in Box 22, provide information on any other vaccines received within one month prior.
2. In Box 18, description of the event:
    a. Write "Pfizer-BioNTech COVID-19 Vaccine 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 with other vaccines.

11 USE IN SPECIFIC POPULATIONS

11.1 Pregnancy

Risk Summary

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 four 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 on the breastfed infant or on milk production/excretion.

11.3 Pediatric Use

Emergency Use Authorization of Pfizer-BioNTech COVID-19 Vaccine in adolescents 12 through 18 years of age is based on safety and effectiveness data in this age group and in adults.

Emergency Use Authorization of Pfizer-BioNTech COVID-19 Vaccine does not include use in individuals younger than 12 years of age.

11.4 Geriatric Use

Clinical studies of Pfizer-BioNTech COVID-19 Vaccine include participants 65 years of age and older and their data contributes to the overall assessment of safety and efficacy *[see Overall Safety Summary (6.1) and Clinical*

Trial Results and Supporting Data for EUA (18.1)]. Of the total number of Pfizer-BioNTech COVID-19 Vaccine recipients in Study 2 (N=20,033), 21.4% (n=4,294) were 65 years of age and older and 4.3% (n=860) were 75 years of age and older.

11.5 Use in Immunocompromised

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, safety and effectiveness of a third dose of the Pfizer-BioNTech COVID-19 vaccine have been evaluated in persons that received solid organ transplants. The administration of a third dose of vaccine appears to be only moderately effective in increasing potentially protective antibody titers. Patients should still be counselled to maintain physical precautions to help prevent COVID-19. In addition, close contacts of immunocompromised persons should be vaccinated as appropriate for their health status.

13 DESCRIPTION

The Pfizer-BioNTech COVID-19 Vaccine is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of the Pfizer-BioNTech COVID-19 Vaccine contains 30 mcg of a nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.

Each dose of the Pfizer-BioNTech COVID-19 Vaccine also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

The Pfizer-BioNTech COVID-19 Vaccine 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 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

18.1 Efficacy 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 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 7 presents the specific demographic characteristics in the studied population.

Table 7: 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)

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 one dose (49 in the vaccine group and 51 in the placebo group). Some of these participants were included in the efficacy evaluation

	Pfizer-BioNTech COVID-19 Vaccine (N=18,242) n (%)	Placebo (N=18,379) n (%)

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 8.

Table 8: 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 N[a]=18,198 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=18,325 Cases n1[b] Surveillance Time[c] (n2[d])**	**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 N[a]=19,965 Cases n1[b] Surveillance Time[c] (n2[d])**	**Placebo N[a]=20,172 Cases n1[b] Surveillance Time[c] (n2[d])**	**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.

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 adolescents 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 in Adolescents 12 Through 15 Years of Age

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

The efficacy information in adolescents 12 through 15 years of age is presented in Table 9.

Table 9: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2: Without Evidence of Infection and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period, Adolescents 12 Through 15 Years of Age Evaluable Efficacy (7 Days) Population

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

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

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

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

18.3 Immunogenicity in Adolescents 12 Through 15 Years of Age

In Study 2, an analysis of SARS-CoV-2 50% neutralizing titers 1 month after Dose 2 in a randomly selected subset of participants demonstrated non-inferior immune responses (within 1.5-fold) comparing adolescents 12 through 15 years of age to participants 16 through 25 years of age who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after Dose 2 (Table 10).

Table 10: Summary of Geometric Mean Ratio for 50% Neutralizing Titer – Comparison of Adolescents 12 Through 15 Years of Age to Participants 16 Through 25 Years of Age (Immunogenicity Subset) –Participants Without Evidence of Infection up to 1 Month After Dose 2 – Dose 2 Evaluable Immunogenicity Population

		Pfizer-BioNTech COVID-19 Vaccine			
		12 Through 15 Years n[a]=190	16 Through 25 Years n[a]=170	12 Through 15 Years/ 16 Through 25 Years	
Assay	Time Point[b]	GMT[c] (95% CI[c])	GMT[c] (95% CI[c])	GMR[d] (95% CI[d])	Met Noninferiority Objective[e] (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)[f]	1 month after Dose 2	1239.5 (1095.5, 1402.5)	705.1 (621.4, 800.2)	1.76 (1.47, 2.10)	Y

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

Note: Participants who had no serological or virological evidence (up to 1 month after receipt of the last dose) 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 up to 1 month after Dose 2 were included in the analysis.

a. n = Number of participants with valid and determinate assay results for the specified assay at the given dose/sampling time point.
b. Protocol-specified timing for blood sample collection.
c. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.
d. GMRs and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titers (Group 1 [12 through 15 years of age] – Group 2 [16 through 25 years of age]) and the corresponding CI (based on the Student t distribution).
e. Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67.
f. SARS-CoV-2 50% neutralization titers (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 in Solid Organ Transplant Recipients

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

19 HOW SUPPLIED/STORAGE AND HANDLING

Pfizer-BioNTech COVID-19 Vaccine Suspension for Intramuscular Injection, Multiple Dose Vials are supplied in a carton containing 25 multiple dose vials (NDC 59267-1000-3) or 195 multiple dose vials (NDC 59267-1000-2). After dilution, one vial contains 6 doses of 0.3 mL. Vial labels and cartons may state that after dilution, a vial contains 5 doses of 0.3 mL. The information in this Full EUA Prescribing Information

regarding the number of doses per vial after dilution supersedes the number of doses stated on vial labels and cartons.

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

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of Pfizer-BioNTech COVID-19 Vaccine Multiple Dose Vials arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90ºC to -60ºC (-130ºF to -76ºF) until the expiry date printed on the label. This information in the package insert supersedes the storage conditions printed on the vial cartons.

Cartons and vials of Pfizer-BioNTech COVID-19 Vaccine with an expiry date of August 2021 through February 2022 printed on the label may remain in use for 3 months beyond the printed date as long as approved storage conditions between -90ºC to -60ºC (-130ºF to -76ºF) have been maintained. Updated expiry dates are shown below.

Printed Expiry Date		Updated Expiry Date
August 2021	→	November 2021
September 2021	→	December 2021
October 2021	→	January 2022
November 2021	→	February 2022
December 2021	→	March 2022
January 2022	→	April 2022
February 2022	→	May 2022

If not stored between -90ºC to -60ºC (-130ºF to -76ºF), vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned one time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which the Pfizer-BioNTech COVID-19 Vaccine arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90ºC to -60ºC (-130ºF to -76ºF). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned one time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2ºC to 8ºC (35ºF to 46ºF)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25ºC (77ºF)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of one or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 12 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.

20 PATIENT COUNSELING INFORMATION

Advise the recipient or caregiver to read the Vaccine Information 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.

Manufactured by
Pfizer Inc., New York, NY 10017

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

LAB-1457-11.4

Revised: 23 August 2021