

FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE (VACCINATION PROVIDERS)

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

The Health Sciences Authority (HSA) has granted an interim authorization to permit the emergency use of the therapeutic product, **Pfizer-BioNTech COVID-19 Vaccine**, for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) in individuals 12 years of age and older.

SUMMARY OF INSTRUCTIONS FOR COVID-19 VACCINATION PROVIDERS

Vaccination providers 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 INTERIM AUTHORIZATION” for reporting requirements.

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

Booster dose

A booster dose of Pfizer-BioNTech COVID-19 Vaccine may be administered intramuscularly after the second dose. The decision when and for whom to implement a booster of Pfizer-BioNTech COVID-19 Vaccine should be made based on available vaccine safety and effectiveness data, in accordance with official recommendations.

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 -90°C to -60°C (-130°F to -76°F) 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 February 2022 through December 2022 printed on the label may remain in use beyond the printed date until the updated expiry date shown below; as long as approved storage conditions between -90°C to -60°C (-130°F to -76°F) have been maintained.

<u>Printed Expiry Date</u>		<u>Updated Expiry Date</u>
02/2022	→	31-Aug-2022
03/2022	→	30-Sep-2022
06/2022	→	30-Sep-2022
07/2022	→	31-Oct-2022
08/2022	→	30-Nov-2022
09/2022	→	31-Dec-2022
10/2022	→	31-Jan-2023
11/2022	→	28-Feb-2023
12/2022	→	31-Mar-2023

If not stored between -90°C to -60°C (-130°F to -76°F), 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 -90°C to -60°C (-130°F to -76°F); not exceeding the expiry date (EXP). 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 -90°C to -60°C (-130°F to -76°F). 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 -90°C to -60°C (-130°F to -76°F); not exceeding the expiry date (EXP).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2°C to 8°C (35°F to 46°F)] for up to 31 days; not exceeding the expiry date (EXP). 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 25°C (77°F)] 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 48 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 primary series of two doses (0.3 mL each) 3 weeks apart.

Booster Dose

A booster dose of Pfizer-BioNTech COVID-19 Vaccine may be administered intramuscularly after the second dose. The decision when and for whom to implement a booster of Pfizer-BioNTech COVID-19 Vaccine should be made based on available vaccine safety and effectiveness data, in accordance with official recommendations.

Interchangeability

The interchangeability of the Pfizer-BioNTech COVID-19 Vaccine with other COVID-19 vaccines to complete the primary vaccination series or the booster dose has not been established. Individuals who have received one dose of Pfizer-BioNTech COVID-19 Vaccine should receive a second dose of Pfizer-BioNTech COVID-19 Vaccine to complete the primary vaccination series and for any additional doses.

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 [2°C to 8°C (35°F to 46°F)] or at room temperature [up to 25°C (77°F)] (see *Storage and Handling*).
- Refer to thawing instructions in the panels below.

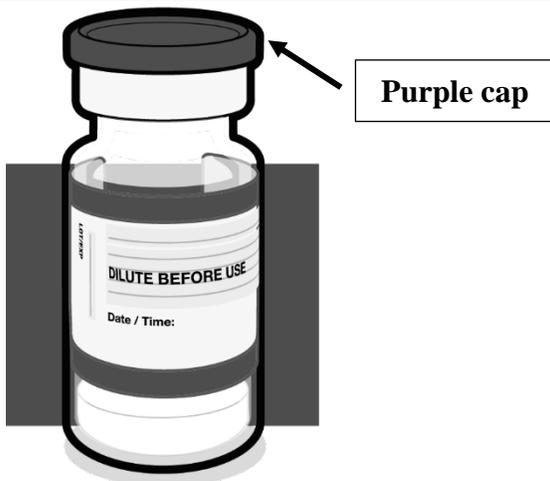
Dilution

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.

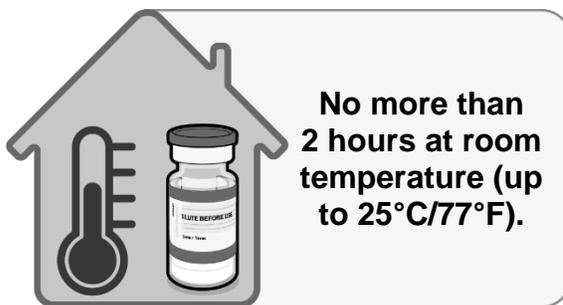
- Refer to dilution and dose preparation instructions in the panels below.

VIAL VERIFICATION

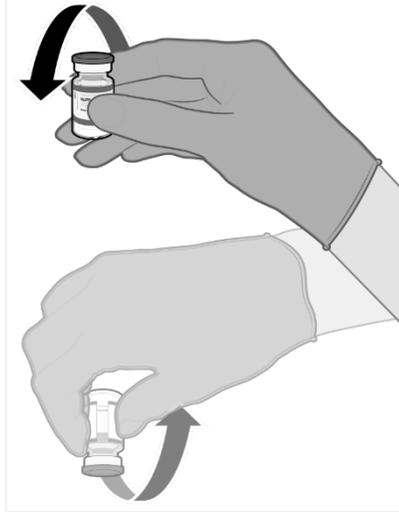


- Verify that the vial has a purple plastic cap. If the vial has a grey plastic cap, refer to the handling instructions for COMIRNATY (For 12 Years of Age and Older) (Vials with Grey Cap). If the vial has an orange plastic cap, refer to the handling instructions for COMIRNATY (For Age 5 Years to <12 Years) (Vials with Orange Cap).

THAWING PRIOR TO DILUTION



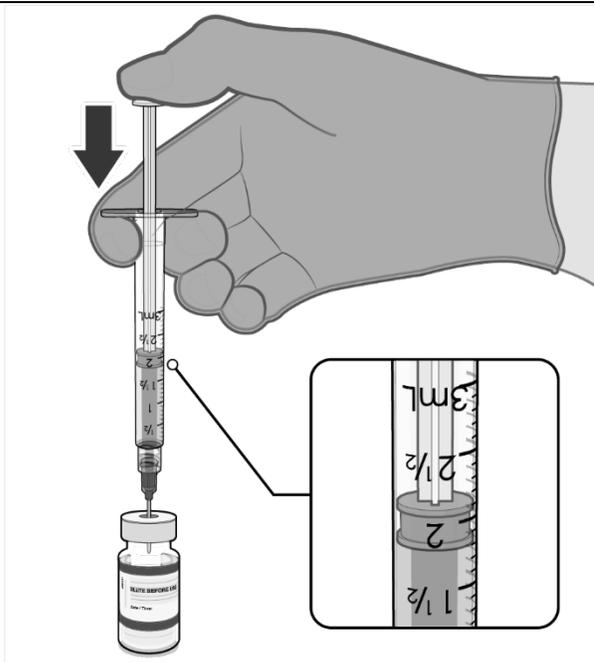
- Thaw vial(s) of Pfizer-BioNTech COVID-19 Vaccine before use either by:
 - Allowing vial(s) to thaw in the refrigerator [2°C to 8°C (35°F to 46°F)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 31 days; not exceeding the expiry date (EXP).
 - Allowing vial(s) to sit at room temperature [up to 25°C (77°F)] for 30 minutes.
- Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.



Gently x 10

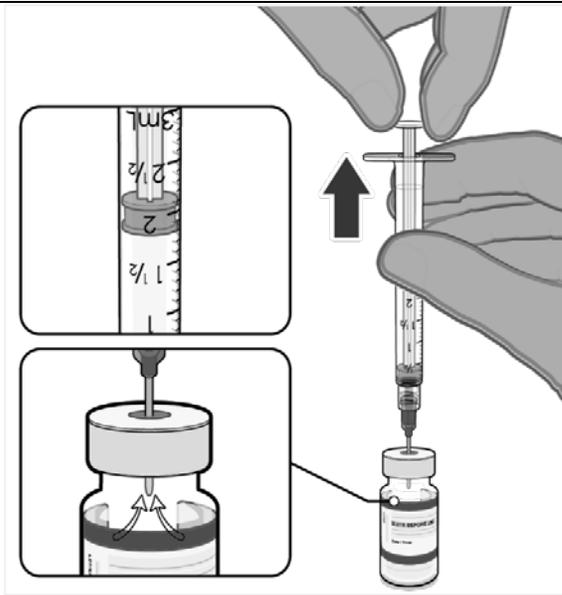
- Before dilution invert vaccine vial gently 10 times.
- Do not shake.
- Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles.
- Do not use if liquid is discolored or if other particles are observed.

DILUTION



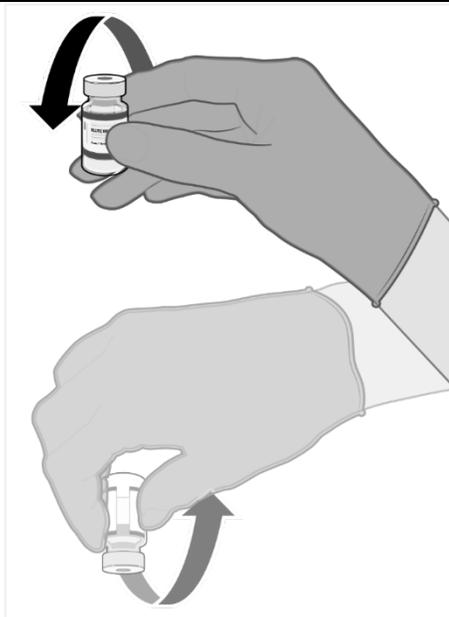
1.8 mL of sterile 0.9% sodium chloride injection, USP

- Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent.
- Using aseptic technique, withdraw 1.8 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.



**Pull back plunger to 1.8 mL to
remove air from vial.**

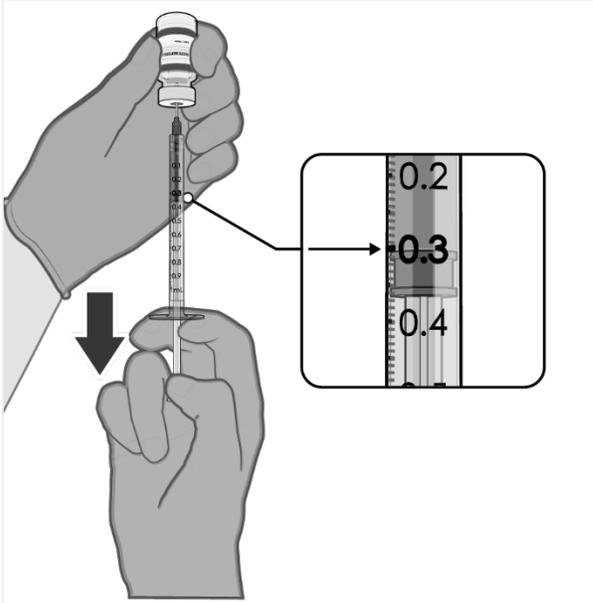
- Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.



Gently × 10

- 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.

 <p>Record appropriate date and time. Use within 6 hours after dilution.</p>	<ul style="list-style-type: none"> • 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.
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<p>PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF PFIZER-BIONTECH COVID-19 VACCINE</p>	
 <p>0.3 mL diluted vaccine</p>	<ul style="list-style-type: none"> • Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw <u>0.3 mL</u> 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 *Prescribing Information*).

Warnings

Management of Acute Allergic Reactions

Vaccine recipients should be observed for at least 30 minutes after vaccination for signs of allergic reactions.

As with any vaccine, 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.

A second dose should not be given to individuals who have experienced anaphylaxis to the first dose.

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. Vaccine recipients should be advised to avoid strenuous physical activity for two weeks after vaccination. They should be advised to seek medical attention promptly if they develop chest pain, shortness of breath or abnormal heartbeats.

Stress-related Responses

Some individuals may have stress-related responses associated with the process

of vaccination itself. Stress-related responses are temporary and resolve on their own. They may include dizziness, fainting, palpitations, increases in heart rate, alterations in blood pressure, feeling short of breath, tingling sensations, sweating and/or anxiety. Individuals should be advised to bring symptoms to the attention of the vaccination provider for evaluation and precautions should be in place to avoid injury from fainting.

The administration of Pfizer-BioNTech COVID-19 Vaccine should be postponed in individuals suffering from acute severe febrile illness.

Individuals receiving anticoagulant therapy or those with a bleeding disorder that would contraindicate intramuscular injection, should not be given Pfizer-BioNTech COVID-19 Vaccine unless the potential benefit clearly outweighs the risk of administration.

Altered Immunocompetence

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

Limitation of Effectiveness

As with any vaccine, Pfizer-BioNTech COVID-19 Vaccine may not protect all vaccine recipients.

Adverse Reactions

Adverse Reactions in Clinical Trials

Adverse reactions following administration of 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, lymphadenopathy, asthenia, decreased appetite, hyperhidrosis, lethargy, and night sweats (*see 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, pericarditis, paresthesia, hypoesthesia, and erythema multiforme 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 “Fact Sheet for Recipients and Caregivers” (and provide a copy or direct the individual to the website www.cvdvaccine.com to obtain the Fact Sheet) prior to the individual receiving each dose of Pfizer-BioNTech COVID-19 Vaccine, including:

- HSA has granted an interim authorization for the use of the Pfizer-BioNTech COVID-19 Vaccine, which is not a HSA-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.

MANDATORY REQUIREMENTS FOR PFIZER-BIONTECH COVID-19 VACCINE ADMINISTRATION UNDER INTERIM AUTHORIZATION

In order to mitigate the risks of using this unapproved product under interim authorization 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 interim authorization 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 “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.
4. The vaccination provider is responsible for mandatory reporting of the following:
 - 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.

The reports should include the words “Pfizer-BioNTech COVID-19 Vaccine Interim Authorization” in the description section of the report.

5. The vaccination provider is responsible for responding to HSA 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 PFIZER SINGAPORE

Vaccination providers may report all other adverse events, to the extent feasible, to Pfizer Singapore using the contact information below.

Email	Fax number	Telephone number
SGP.AEReporting@pfizer.com	8001012817 (local toll free)	+65 6403 8888

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
<p data-bbox="363 573 670 604">www.cvdvaccine.com</p> 	<p data-bbox="1003 642 1206 674">+65 6403 8888</p>

MEDICAL INFORMATION ENQUIRIES – Singapore

Please submit your medical information enquiries at <https://pmiform.com/HCP/SG>. Alternatively, you may send them to MedicalInformationSingapore@pfizer.com.

AVAILABLE ALTERNATIVES

There is currently no approved alternative vaccine in Singapore to prevent COVID-19. There may be clinical trials or availability under interim authorization of other COVID-19 vaccines.

AUTHORITY FOR ISSUANCE OF THE INTERIM AUTHORIZATION

The interim authorization for the abovementioned emergency therapeutic product by the Health Sciences Authority (HSA) of Singapore is made under Regulations 60A(4) and (5)(b) of the Health Product (Therapeutic Products) Regulations.

HSA issued this interim authorization, based on Pfizer-BioNTech's request and submitted data.

For 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 may be effective for the prevention of COVID-19 in individuals as specified in the *Prescribing Information*.

For additional information about Interim Authorization, visit HSA at: <https://www.hsa.gov.sg/therapeutic-products/register/special-access-routes/psar-emergency-therapeutic-product>.

BIONTECH

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



Manufactured by
Pfizer Inc., New York, NY 10017

Reference label: CDS version 12.0

Revised: 03 August 2022

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

INTERIM AUTHORIZATION PRESCRIBING INFORMATION

PFIZER-BIONTECH COVID-19 VACCINE

INTERIM 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 Stress-related Responses
 - 5.4 Concurrent Illness at Time of Vaccination
 - 5.5 Bleeding Precautions
 - 5.6 Altered Immunocompetence
 - 5.7 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
- 13 DESCRIPTION**
- 14 CLINICAL PHARMACOLOGY**
 - 14.1 Mechanism of Action
- 18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR
INTERIM AUTHORIZATION**
 - 18.1 Efficacy in Participants 16 Years of Age and Older – After 2 Doses
 - 18.2 Efficacy in Adolescents 12 Through 15 Years of Age – After 2
Doses
 - 18.3 Immunogenicity in Adolescents 12 Through 15 Years of Age –
After 2 Doses
 - 18.4 Immunogenicity in Participants 18 Years of Age and older – After
Booster Dose
 - 18.5 Relative Vaccine Efficacy in Participants 16 Years of Age and
Older – After Booster Dose
- 19 HOW SUPPLIED/STORAGE AND HANDLING**
- 20 PATIENT COUNSELING INFORMATION**
- 21 CONTACT INFORMATION**

* Sections or subsections omitted from the interim authorization prescribing information are not listed.

INTERIM AUTHORIZATION PRESCRIBING INFORMATION

1 AUTHORIZED USE

Pfizer-BioNTech COVID-19 Vaccine is authorized for use under an Interim Authorization 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

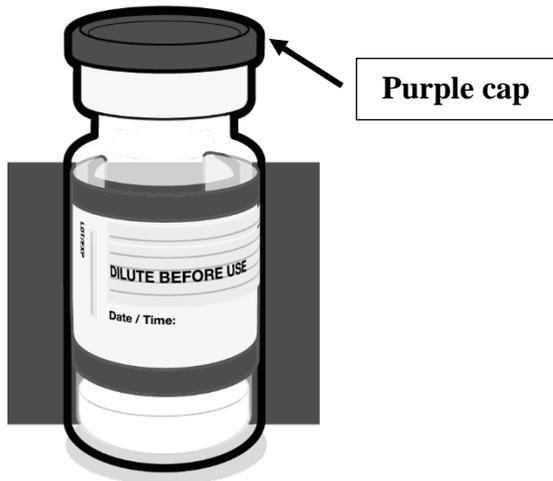
Prior to Dilution

- 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 [2°C to 8°C (35°F to 46°F)] or at room temperature [up to 25°C (77°F)] [*see How Supplied/Storage and Handling (19)*].
- Refer to thawing instructions in the panels below.

Dilution

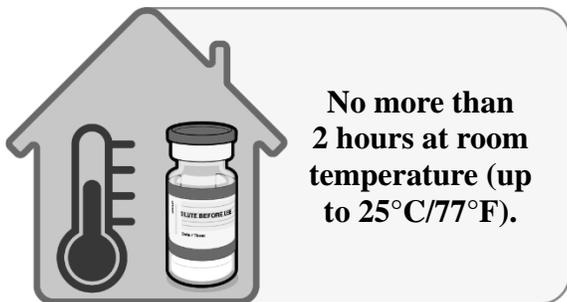
- Dilute the vial contents using 1.8 mL of 0.9% Sodium Chloride Injection, USP (not provided) to form the Pfizer-BioNTech COVID-19 Vaccine. Do not add more than 1.8 mL of diluent.
- **ONLY** use 0.9% Sodium Chloride Injection, USP as the diluent. This diluent is not packaged with the vaccine and must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

VIAL VERIFICATION

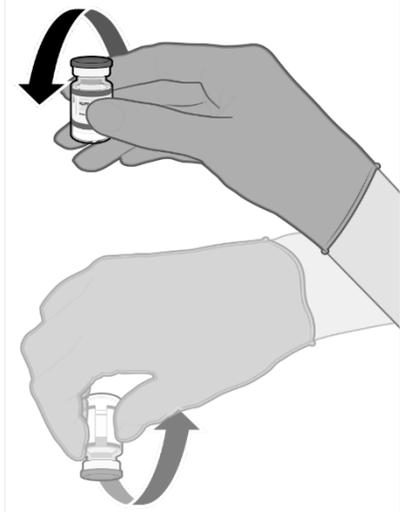


- Verify that the vial has a purple plastic cap. If the vial has a grey plastic cap, refer to the handling instructions for COMIRNATY (For 12 Years of Age and Older) (Vials with Grey Cap). If the vial has an orange plastic cap, refer to the handling instructions for COMIRNATY (For Age 5 Years to <12 Years) (Vials with Orange Cap).

THAWING PRIOR TO DILUTION



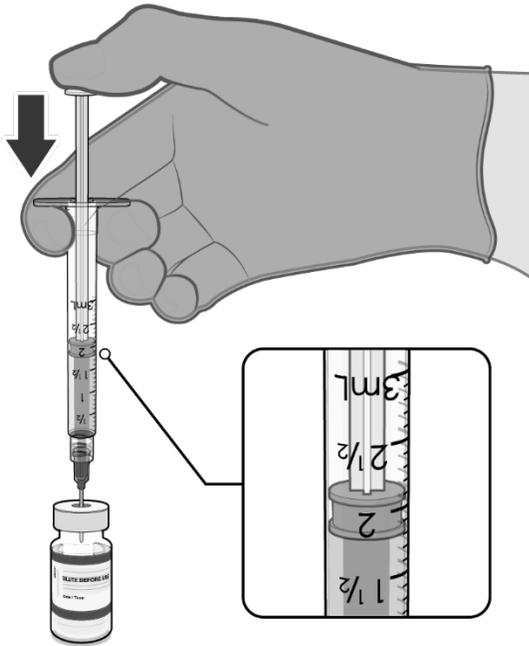
- Thaw vial(s) of Pfizer-BioNTech COVID-19 Vaccine before use either by:
 - Allowing vial(s) to thaw in the refrigerator [2°C to 8°C (35°F to 46°F)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 31 days; not exceeding the expiry date (EXP).
 - Allowing vial(s) to sit at room temperature [up to 25°C (77°F)] for 30 minutes.
- Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.



Gently × 10

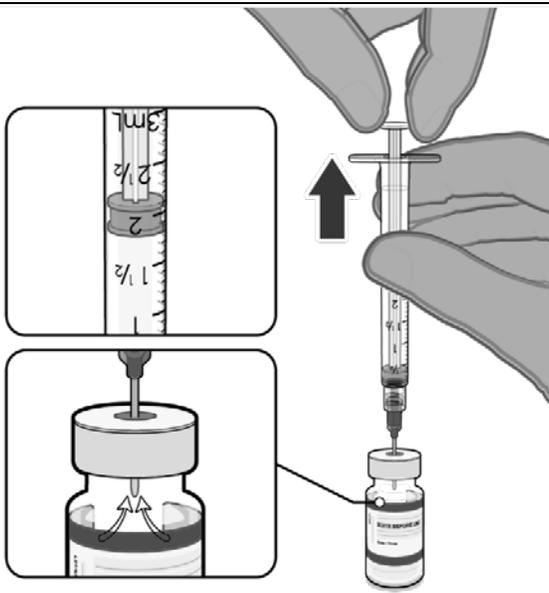
- Before dilution invert vaccine vial gently 10 times.
- Do not shake.
- Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles.
- Do not use if liquid is discolored or if other particles are observed.

DILUTION



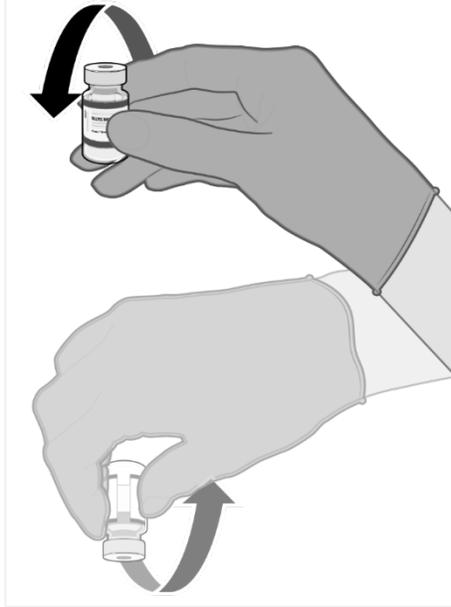
1.8 mL of sterile 0.9% sodium chloride injection, USP

- Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent.
- Using aseptic technique, withdraw 1.8 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.



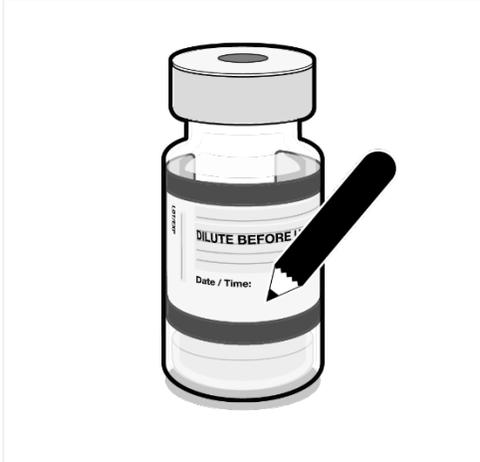
Pull back plunger to 1.8 mL to remove air from vial.

- Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.



Gently × 10

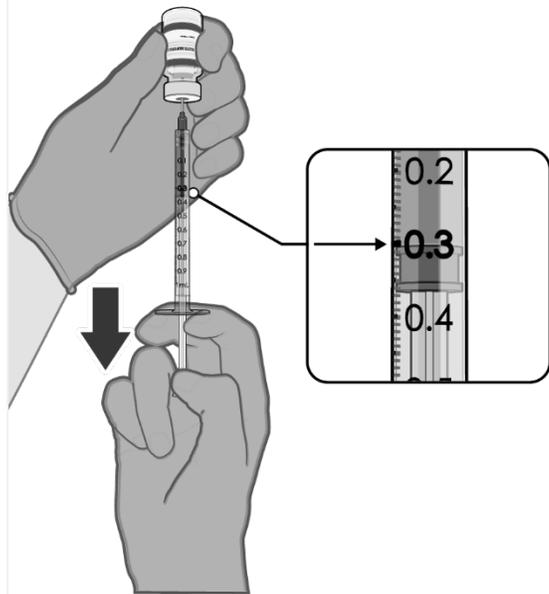
- Gently invert the vial containing the Pfizer-BioNTech COVID-19 Vaccine 10 times to mix.
- Do not shake.
- Inspect the vaccine in the vial.
- The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.



**Record appropriate date and time.
Use within 6 hours after dilution.**

- 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



0.3 mL diluted 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 primary series of two doses (0.3 mL each) three weeks apart.

Booster Dose

A booster dose of Pfizer-BioNTech COVID-19 Vaccine may be administered intramuscularly after the second dose. The decision when and for whom to implement a booster of Pfizer-BioNTech COVID-19 Vaccine should be made based on available vaccine safety and effectiveness data, in accordance with official recommendations.

Interchangeability

The interchangeability of the Pfizer-BioNTech COVID-19 Vaccine with other COVID-19 vaccines to complete the primary vaccination series or the booster dose has not been established. Individuals who have received one dose of Pfizer-BioNTech COVID-19 Vaccine should receive a second dose of Pfizer-BioNTech COVID-19 Vaccine to complete the primary vaccination series and for any additional doses.

3 DOSAGE FORMS AND STRENGTHS

Pfizer-BioNTech COVID-19 Vaccine is a suspension for injection. After preparation, a single dose is 0.3 mL [*see Dosage and Administration (2.1)*].

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

Vaccine recipients should be observed for at least 30 minutes after vaccination for signs of allergic reactions.

As with any vaccine, 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.

A second dose should not be given to individuals who have experienced anaphylaxis to the first dose.

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. Vaccine recipients should be advised to avoid strenuous physical activity for two weeks after vaccination. They should be advised to seek medical attention promptly if they develop chest pain, shortness of breath or abnormal heartbeats.

5.3 Stress-related Responses

Some individuals may have stress-related responses associated with the process of vaccination itself. Stress-related responses are temporary and resolve on their own. They may include dizziness, fainting, palpitations, increases in heart rate, alterations in blood pressure, feeling short of breath, tingling sensations, sweating and/or anxiety. Individuals should be advised to bring symptoms to the attention of the vaccination provider for evaluation and precautions should be in place to avoid injury from fainting.

5.4 Concurrent Illness at Time of Vaccination

The administration of Pfizer-BioNTech COVID-19 Vaccine should be postponed in individuals suffering from acute severe febrile illness.

5.5 Bleeding Precautions

Individuals receiving anticoagulant therapy or those with a bleeding disorder that would contraindicate intramuscular injection, should not be given Pfizer-BioNTech COVID-19 Vaccine unless the potential benefit clearly outweighs the risk of administration.

5.6 Altered Immunocompetence

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

5.7 Limitation of Effectiveness

As with any vaccine, Pfizer-BioNTech COVID-19 Vaccine may not protect all vaccine recipients.

6 OVERALL SAFETY SUMMARY

It is MANDATORY for vaccination providers to report 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.

In clinical studies with a data cut-off of March 13, 2021, adverse reactions in participants 16 years of age and older that received 2 doses included pain at the injection site (84.3%), fatigue (64.7%), headache (57.1%), muscle pain (40.2%), chills (34.7%), joint pain (25.0%), fever (15.2%), injection site swelling (11.1%), injection site redness (9.9%), nausea (1.2%), malaise (0.6%), lymphadenopathy (0.4%), asthenia (0.3%), decreased appetite (0.2%), hyperhidrosis (0.1%), lethargy (0.1%), and night sweats (0.1%).

In a clinical study, adverse reactions in adolescents 12 through 15 years of age that received 2 doses 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%).

A higher frequency of pyrexia was observed after the second dose compared to the first dose.

Additionally, 306 existing Phase 3 participants least 18 through 55 years of age received a booster dose of Pfizer-BioNTech COVID-19 Vaccine approximately 6 months after the second dose in the non-placebo-

controlled booster dose portion of Study 2. The overall safety profile for the booster dose was similar to that seen after 2 doses. The most frequent adverse reactions following administration of a booster dose were injection site pain (> 80%), fatigue (> 60%), headache (> 40%), myalgia (> 30%), chills and arthralgia (> 20%).

In Study C4591031 (Study 4), a placebo-controlled booster study, 5,081 participants 16 years of age and older were recruited from Study 2 to receive a booster dose of Pfizer-BioNTech COVID-19 Vaccine at least 6 months after the second dose. The overall safety profile for the booster dose was similar to that seen after 2 doses.

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 the primary series 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 and 36 participants, 56 through 85 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 44,047 participants (22,026 Pfizer-BioNTech COVID-19 Vaccine; 22,021 placebo) in Phase 2/3 are 16 years of age or older (including 378 and 376 adolescents 16 through 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). Study 2 also included 200 participants with confirmed stable human immunodeficiency virus (HIV) infection; HIV-positive participants are included in safety population disposition but are summarized separately in safety analyses.

A subset from Study 2 Phase 2/3 participants of 306 adults at least 18 through 55 years of age who completed the primary Pfizer-BioNTech COVID-19 Vaccine 2-dose course, received a booster dose of Pfizer-BioNTech COVID-19 Vaccine approximately 6 months (range of 4.8 to 8.0 months) after receiving Dose 2.

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 8 present the frequency and severity of reported 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 – After 2 Doses

At the time of the analysis of Study 2 for the interim authorization with a data cut-off of November 14, 2020, there were 37,586 participants (18,801 Pfizer-BioNTech COVID-19 Vaccine and 18,785 placebo) 16 years of

age or older followed for a median of 2 months after the second dose of Pfizer-BioNTech COVID-19 Vaccine. At the time of the analysis of Study 2 for the interim authorization with a data cut-off of March 13, 2021, there were 25,651 (58.2%) participants (13,031 Pfizer-BioNTech COVID-19 Vaccine and 12,620 placebo) 16 years of age and older were followed up for ≥ 4 months after the second dose.

The safety evaluation in Study 2 is ongoing. The safety population includes participants 16 years of age and older enrolled by October 9, 2020, and includes safety data accrued through March 13, 2021.

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 Pfizer-BioNTech COVID-19 Vaccine or placebo, 50.9% were male and 49.1% were female, 82.0% were White, 9.6% were Black or African American, 25.9% were Hispanic/Latino, 4.3% were Asian, and 1.0% were American Indian or Alaska Native.

Solicited Local and Systemic Adverse Reactions

In participants 16 through 55 years of age after receiving Dose 2, the mean duration of pain at the injection site was 2.5 days (range 1 to 70 days), for redness 2.2 days (range 1 to 9 days), and for swelling 2.1 days (range 1 to 8 days) for participants in the Pfizer-BioNTech COVID-19 Vaccine group. In participants 56 years of age and older after receiving Dose 2, the mean duration of pain at the injection site was 2.4 days (range 1 to 36 days), for redness 3.0 days (range 1 to 34 days), and for swelling 2.6 days (range 1 to 34 days) for participants in the Pfizer-BioNTech COVID-19 Vaccine group.

Table 1: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine Dose 1 N^a=2899 n^b (%)	Placebo Dose 1 N^a=2908 n^b (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N^a=2682 n^b (%)	Placebo Dose 2 N^a=2684 n^b (%)
Redness^c				
Any (>2.0 cm)	156 (5.4)	28 (1.0)	151 (5.6)	18 (0.7)
Mild	113 (3.9)	19 (0.7)	90 (3.4)	12 (0.4)
Moderate	36 (1.2)	6 (0.2)	50 (1.9)	6 (0.2)
Severe	7 (0.2)	3 (0.1)	11 (0.4)	0
Swelling^c				
Any (>2.0 cm)	184 (6.3)	16 (0.6)	183 (6.8)	5 (0.2)
Mild	124 (4.3)	6 (0.2)	110 (4.1)	3 (0.1)
Moderate	54 (1.9)	8 (0.3)	66 (2.5)	2 (0.1)
Severe	6 (0.2)	2 (0.1)	7 (0.3)	0

	Pfizer-BioNTech COVID-19 Vaccine Dose 1 N^a=2899 n^b (%)	Placebo Dose 1 N^a=2908 n^b (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N^a=2682 n^b (%)	Placebo Dose 2 N^a=2684 n^b (%)
Pain at the injection site^d				
Any	2426 (83.7)	414 (14.2)	2101 (78.3)	312 (11.6)
Mild	1464 (50.5)	391 (13.4)	1274 (47.5)	284 (10.6)
Moderate	923 (31.8)	20 (0.7)	788 (29.4)	28 (1.0)
Severe	39 (1.3)	3 (0.1)	39 (1.5)	0

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

No Grade 4 solicited local reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

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.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 16 Through 55 Years of Age – Reactogenicity Subset of the Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine Dose 1 N^a=2899 n^b (%)	Placebo Dose 1 N^a=2908 n^b (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N^a=2682 n^b (%)	Placebo Dose 2 N^a=2684 n^b (%)
Fever				
≥38.0°C	119 (4.1)	25 (0.9)	440 (16.4)	11 (0.4)
≥38.0°C to 38.4°C	86 (3.0)	16 (0.6)	254 (9.5)	5 (0.2)
>38.4°C to 38.9°C	25 (0.9)	5 (0.2)	146 (5.4)	4 (0.1)
>38.9°C to 40.0°C	8 (0.3)	4 (0.1)	39 (1.5)	2 (0.1)
>40.0°C	0	0	1 (0.0)	0
Fatigue^c				
Any	1431 (49.4)	960 (33.0)	1649 (61.5)	614 (22.9)
Mild	760 (26.2)	570 (19.6)	558 (20.8)	317 (11.8)
Moderate	630 (21.7)	372 (12.8)	949 (35.4)	283 (10.5)
Severe	41 (1.4)	18 (0.6)	142 (5.3)	14 (0.5)
Headache^c				
Any	1262 (43.5)	975 (33.5)	1448 (54.0)	652 (24.3)
Mild	785 (27.1)	633 (21.8)	699 (26.1)	404 (15.1)
Moderate	444 (15.3)	318 (10.9)	658 (24.5)	230 (8.6)
Severe	33 (1.1)	24 (0.8)	91 (3.4)	18 (0.7)
Chills^c				
Any	479 (16.5)	199 (6.8)	1015 (37.8)	114 (4.2)
Mild	338 (11.7)	148 (5.1)	477 (17.8)	89 (3.3)
Moderate	126 (4.3)	49 (1.7)	469 (17.5)	23 (0.9)
Severe	15 (0.5)	2 (0.1)	69 (2.6)	2 (0.1)

	Pfizer-BioNTech COVID-19 Vaccine Dose 1 N^a=2899 n^b (%)	Placebo Dose 1 N^a=2908 n^b (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N^a=2682 n^b (%)	Placebo Dose 2 N^a=2684 n^b (%)
Vomiting^d				
Any	34 (1.2)	36 (1.2)	58 (2.2)	30 (1.1)
Mild	29 (1.0)	30 (1.0)	42 (1.6)	20 (0.7)
Moderate	5 (0.2)	5 (0.2)	12 (0.4)	10 (0.4)
Severe	0	1 (0.0)	4 (0.1)	0
Diarrhea^e				
Any	309 (10.7)	323 (11.1)	269 (10.0)	205 (7.6)
Mild	251 (8.7)	264 (9.1)	219 (8.2)	169 (6.3)
Moderate	55 (1.9)	58 (2.0)	44 (1.6)	35 (1.3)
Severe	3 (0.1)	1 (0.0)	6 (0.2)	1 (0.0)
New or worsened muscle pain^c				
Any	664 (22.9)	329 (11.3)	1055 (39.3)	237 (8.8)
Mild	353 (12.2)	231 (7.9)	441 (16.4)	150 (5.6)
Moderate	296 (10.2)	96 (3.3)	552 (20.6)	84 (3.1)
Severe	15 (0.5)	2 (0.1)	62 (2.3)	3 (0.1)
New or worsened joint pain^c				
Any	342 (11.8)	168 (5.8)	638 (23.8)	147 (5.5)
Mild	200 (6.9)	112 (3.9)	291 (10.9)	82 (3.1)
Moderate	137 (4.7)	55 (1.9)	320 (11.9)	61 (2.3)
Severe	5 (0.2)	1 (0.0)	27 (1.0)	4 (0.1)
Use of antipyretic or pain medication^f	805 (27.8)	398 (13.7)	1213 (45.2)	320 (11.9)

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

No Grade 4 solicited systemic reactions were reported in participants 16 through 55 years of age.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

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.

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=2008 n^b (%)	Placebo Dose 1 N^a=1989 n^b (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N^a=1860 n^b (%)	Placebo Dose 2 N^a=1833 n^b (%)
Redness^c				
Any (>2.0 cm)	106 (5.3)	20 (1.0)	133 (7.2)	14 (0.8)
Mild	71 (3.5)	13 (0.7)	65 (3.5)	10 (0.5)
Moderate	30 (1.5)	5 (0.3)	58 (3.1)	3 (0.2)
Severe	5 (0.2)	2 (0.1)	10 (0.5)	1 (0.1)
Swelling^c				
Any (>2.0 cm)	141 (7.0)	23 (1.2)	145 (7.8)	13 (0.7)
Mild	87 (4.3)	11 (0.6)	80 (4.3)	5 (0.3)
Moderate	52 (2.6)	12 (0.6)	61 (3.3)	7 (0.4)
Severe	2 (0.1)	0	4 (0.2)	1 (0.1)
Pain at the injection site^d				
Any (>2.0 cm)	1408 (70.1)	185 (9.3)	1230 (66.1)	143 (7.8)
Mild	1108 (55.2)	177 (8.9)	873 (46.9)	138 (7.5)
Moderate	296 (14.7)	8 (0.4)	347 (18.7)	5 (0.3)
Severe	4 (0.2)	0	10 (0.5)	0

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

No Grade 4 solicited local reactions were reported in participants 56 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, the information was included in the column header.

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.

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=2008 n^b (%)	Placebo Dose 1 N^a=1989 n^b (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N^a=1860 n^b (%)	Placebo Dose 2 N^a=1833 n^b (%)
Fever				
≥38.0°C	26 (1.3)	8 (0.4)	219 (11.8)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.1)	3 (0.2)	158 (8.5)	2 (0.1)
>38.4°C to 38.9°C	2 (0.1)	3 (0.2)	54 (2.9)	1 (0.1)
>38.9°C to 40.0°C	1 (0.0)	2 (0.1)	7 (0.4)	1 (0.1)
>40.0°C	0	0	0	0
Fatigue^c				
Any	677 (33.7)	447 (22.5)	949 (51.0)	306 (16.7)
Mild	415 (20.7)	281 (14.1)	391 (21.0)	183 (10.0)

	Pfizer-BioNTech COVID-19 Vaccine Dose 1 N^a=2008 n^b (%)	Placebo Dose 1 N^a=1989 n^b (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N^a=1860 n^b (%)	Placebo Dose 2 N^a=1833 n^b (%)
Moderate	259 (12.9)	163 (8.2)	497 (26.7)	121 (6.6)
Severe	3 (0.1)	3 (0.2)	60 (3.2)	2 (0.1)
Grade 4	0	0	1 (0.1)	0
Headache^c				
Any	503 (25.0)	363 (18.3)	733 (39.4)	259 (14.1)
Mild	381 (19.0)	267 (13.4)	464 (24.9)	189 (10.3)
Moderate	120 (6.0)	93 (4.7)	256 (13.8)	65 (3.5)
Severe	2 (0.1)	3 (0.2)	13 (0.7)	5 (0.3)
Chills^c				
Any	130 (6.5)	69 (3.5)	435 (23.4)	57 (3.1)
Mild	102 (5.1)	49 (2.5)	229 (12.3)	45 (2.5)
Moderate	28 (1.4)	19 (1.0)	185 (9.9)	12 (0.7)
Severe	0	1 (0.1)	21 (1.1)	0
Vomiting^d				
Any	10 (0.5)	9 (0.5)	13 (0.7)	5 (0.3)
Mild	9 (0.4)	9 (0.5)	10 (0.5)	5 (0.3)
Moderate	1 (0.0)	0	1 (0.1)	0
Severe	0	0	2 (0.1)	0
Diarrhea^e				
Any	168 (8.4)	130 (6.5)	152 (8.2)	102 (5.6)
Mild	137 (6.8)	109 (5.5)	125 (6.7)	76 (4.1)
Moderate	27 (1.3)	20 (1.0)	25 (1.3)	22 (1.2)
Severe	4 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain^c				
Any	274 (13.6)	165 (8.3)	537 (28.9)	99 (5.4)
Mild	183 (9.1)	111 (5.6)	229 (12.3)	65 (3.5)
Moderate	90 (4.5)	51 (2.6)	288 (15.5)	33 (1.8)
Severe	1 (0.0)	3 (0.2)	20 (1.1)	1 (0.1)
New or worsened joint pain^c				
Any	175 (8.7)	124 (6.2)	353 (19.0)	72 (3.9)
Mild	119 (5.9)	78 (3.9)	183 (9.8)	44 (2.4)
Moderate	53 (2.6)	45 (2.3)	161 (8.7)	27 (1.5)
Severe	3 (0.1)	1 (0.1)	9 (0.5)	1 (0.1)
Use of antipyretic or pain medication^f	382 (19.0)	224 (11.3)	688 (37.0)	170 (9.3)

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

The only Grade 4 solicited systemic reaction reported in participants 56 years of age and older was fatigue.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

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

	Pfizer-BioNTech COVID-19 Vaccine Dose 1 N^a=2008 n^b (%)	Placebo Dose 1 N^a=1989 n^b (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N^a=1860 n^b (%)	Placebo Dose 2 N^a=1833 n^b (%)
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- c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity; Grade 4 reactions were defined in the clinical study protocol as emergency room visit or hospitalization for severe fatigue, severe headache, severe chills, severe muscle pain, or severe joint pain.
- d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration; Grade 4 emergency visit or hospitalization for severe vomiting.
- e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours; Grade 4: emergency room or hospitalization for severe diarrhea.
- f. Severity was not collected for use of antipyretic or pain medication.

Table 5 and Table 6 present the frequency and severity of reported solicited local and systemic reactions, respectively, within 7 days of each dose of Pfizer-BioNTech COVID-19 Vaccine and placebo for participants 16 years of age and older with confirmed stable HIV infection.

Table 5: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine Dose 1 N^a=54 n^b (%)	Placebo Dose 1 N^a=56 n^b (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N^a=60 n^b (%)	Placebo Dose 2 N^a=62 n^b (%)
Redness^c				
Any (>2.0 cm)	2 (3.7)	3 (5.4)	4 (6.7)	1 (1.6)
Mild	2 (3.7)	1 (1.8)	3 (5.0)	1 (1.6)
Moderate	0	0	1 (1.7)	0
Severe	0	2 (3.6)	0	0
Swelling^c				
Any (>2.0 cm)	3 (5.6)	1 (1.8)	5 (8.3)	0
Mild	2 (3.7)	0	2 (3.3)	0
Moderate	1 (1.9)	0	3 (5.0)	0
Severe	0	1 (1.8)	0	0
Pain at the injection site^d				
Any	34 (63.0)	9 (16.1)	32 (53.3)	5 (8.1)
Mild	26 (48.1)	8 (14.3)	22 (36.7)	5 (8.1)
Moderate	8 (14.8)	1 (1.8)	9 (15.0)	0
Severe	0	0	1 (1.7)	0

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

No Grade 4 solicited local reactions were reported in HIV-positive participants 16 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction was the same, therefore, this information was included in the column header.

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.

Table 6: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – HIV-Positive Participants 16 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine Dose 1 N^a=54 n^b (%)	Placebo Dose 1 N^a=56 n^b (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N^a=60 n^b (%)	Placebo Dose 2 N^a=62 n^b (%)
Fever				
≥38.0°C	1 (1.9)	4 (7.1)	9 (15.0)	5 (8.1)
≥38.0°C to 38.4°C	1 (1.9)	2 (3.6)	4 (6.7)	5 (8.1)
>38.4°C to 38.9°C	0	0	4 (6.7)	0
>38.9°C to 40.0°C	0	2 (3.6)	1 (1.7)	0
>40.0°C	0	0	0	0
Fatigue^c				
Any	22 (40.7)	15 (26.8)	24 (40.0)	12 (19.4)
Mild	15 (27.8)	9 (16.1)	12 (20.0)	5 (8.1)
Moderate	7 (13.0)	5 (8.9)	9 (15.0)	7 (11.3)
Severe	0	1 (1.8)	3 (5.0)	0
Headache^c				
Any	11 (20.4)	18 (32.1)	18 (30.0)	12 (19.4)
Mild	7 (13.0)	10 (17.9)	8 (13.3)	8 (12.9)
Moderate	4 (7.4)	7 (12.5)	8 (13.3)	4 (6.5)
Severe	0	1 (1.8)	2 (3.3)	0
Chills^c				
Any	6 (11.1)	5 (8.9)	14 (23.3)	4 (6.5)
Mild	5 (9.3)	4 (7.1)	5 (8.3)	3 (4.8)
Moderate	1 (1.9)	1 (1.8)	8 (13.3)	1 (1.6)
Severe	0	0	1 (1.7)	0
Vomiting^d				
Any	1 (1.9)	3 (5.4)	2 (3.3)	2 (3.2)
Mild	1 (1.9)	1 (1.8)	1 (1.7)	1 (1.6)
Moderate	0	0	1 (1.7)	1 (1.6)
Severe	0	2 (3.6)	0	0
Diarrhea^e				
Any	5 (9.3)	8 (14.3)	4 (6.7)	9 (14.5)
Mild	5 (9.3)	6 (10.7)	1 (1.7)	6 (9.7)
Moderate	0	1 (1.8)	2 (3.3)	3 (4.8)
Severe	0	1 (1.8)	1 (1.7)	0
New or worsened muscle pain^c				
Any	9 (16.7)	10 (17.9)	10 (16.7)	5 (8.1)
Mild	7 (13.0)	7 (12.5)	5 (8.3)	1 (1.6)
Moderate	2 (3.7)	3 (5.4)	5 (8.3)	4 (6.5)
Severe	0	0	0	0

	Pfizer-BioNTech COVID-19 Vaccine Dose 1 N^a=54 n^b (%)	Placebo Dose 1 N^a=56 n^b (%)	Pfizer-BioNTech COVID-19 Vaccine Dose 2 N^a=60 n^b (%)	Placebo Dose 2 N^a=62 n^b (%)
New or worsened joint pain ^c				
Any	5 (9.3)	7 (12.5)	10 (16.7)	5 (8.1)
Mild	5 (9.3)	4 (7.1)	4 (6.7)	1 (1.6)
Moderate	0	3 (5.4)	6 (10.0)	4 (6.5)
Severe	0	0	0	0
Use of antipyretic or pain medication ^f	7 (13.0)	8 (14.3)	16 (26.7)	7 (11.3)

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

No Grade 4 solicited systemic reactions were reported in HIV-positive participants 16 years of age and older.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

a. N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose. The N for each reaction or use of antipyretic or pain medication was the same, therefore, this information was included in the column header.

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

c. Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

d. Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

e. Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

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

Unsolicited Adverse Events

Upon approval of the interim authorization for Pfizer-BioNTech COVID-19 Vaccine, participants were unblinded to offer placebo participants Pfizer-BioNTech COVID-19 Vaccine. Adverse events are reported as incidence rates per 100 person-years to account for the variable exposure since unblinding began in a phased manner for participants in the study. Adverse events detailed below for participants 16 years of age and older are for the placebo-controlled blinded follow-up period up to the participants' unblinding dates.

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 = 12,995; placebo = 13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 2.1 per 100 person-years among Pfizer-BioNTech COVID-19 Vaccine recipients and 2.4 per 100 person-years among placebo recipients. In a similar analysis, in participants 56 years of age and older (Pfizer-BioNTech COVID-19 Vaccine = 8,931, placebo = 8,895), serious adverse events were reported at an incidence rate of 4.9 per 100 person-years among Pfizer-BioNTech COVID-19 Vaccine recipients and 4.6 per 100 person-years among placebo recipients who received at least 1 dose of Pfizer-BioNTech COVID-19 Vaccine or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. Among participants with confirmed stable HIV infection serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 6.6 per 100 person-years among Pfizer-BioNTech COVID-19 Vaccine recipients and 6.9 per 100 person-years among placebo recipients.

There were no notable patterns 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 12,995 participants 16 through 55 years of age received Pfizer-BioNTech COVID-19 Vaccine and 13,026 participants received placebo, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 88.4 per 100 person-years among participants who received Pfizer-BioNTech COVID-19 Vaccine and 43.5 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. In a similar analysis, in participants 56 years of age and older (Pfizer-BioNTech COVID-19 Vaccine = 8,931, placebo = 8,895), all events, which include non-serious adverse events were reported at an incidence rate of 75.7 per 100 person-years among participants who received Pfizer-BioNTech COVID-19 Vaccine and 43.3 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose. Among participants with confirmed stable HIV infection, all events, which include non-serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported at an incidence rate of 95.8 per 100 person-years among participants who received Pfizer-BioNTech COVID-19 Vaccine and 52.0 per 100 person-years among participants in the placebo group, for participants who received at least 1 dose.

In these analyses, 58.2% of study participants had at least 4 months of follow-up after Dose 2. The higher frequency of reported unsolicited non-serious adverse events among Pfizer-BioNTech COVID-19 Vaccine recipients (inclusive of stable HIV infection) compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following each dose of vaccine that are consistent with adverse reactions solicited among participants in the reactogenicity subset and presented in Tables 3 and 4.

Throughout the placebo-controlled safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the Pfizer-BioNTech COVID-19 Vaccine group and 2 participants in the placebo 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. In the placebo group the onset of facial paralysis was Day 32 and Day 102. 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 – After 2 Doses

In an analysis of long-term safety follow-up in Study 2, 2,260 adolescents (1,131 Pfizer-BioNTech COVID-19 Vaccine; 1,129 placebo) were 12 through 15 years of age. Of these, 1,559 (786 Pfizer-BioNTech COVID-19 Vaccine and 773 placebo) adolescents have been followed for ≥ 4 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 7: 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)
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 8: 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)

	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 (%)
Headache^c				
Any	623 (55.3)	396 (35.1)	708 (64.5)	263 (24.4)
Mild	361 (32.0)	256 (22.7)	302 (27.5)	169 (15.7)
Moderate	251 (22.3)	131 (11.6)	384 (35.0)	93 (8.6)
Severe	11 (1.0)	9 (0.8)	22 (2.0)	1 (0.1)
Chills^c				
Any	311 (27.6)	109 (9.7)	455 (41.5)	73 (6.8)
Mild	195 (17.3)	82 (7.3)	221 (20.1)	52 (4.8)
Moderate	111 (9.8)	25 (2.2)	214 (19.5)	21 (1.9)
Severe	5 (0.4)	2 (0.2)	20 (1.8)	0 (0.0)
Vomiting^d				
Any	31 (2.8)	10 (0.9)	29 (2.6)	12 (1.1)
Mild	30 (2.7)	8 (0.7)	25 (2.3)	11 (1.0)
Moderate	0 (0.0)	2 (0.2)	4 (0.4)	1 (0.1)
Severe	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
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: Reactions 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 reaction 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. Psychiatric-related serious adverse events were numerically higher in the vaccine group, 4 recipients (3 [0.3%] with depression and 1 [0.1%] with suicidal ideation) and none in the placebo group. The events in the vaccine group were confounded by prior medical history as all 4 participants had concurrent psychiatric illness including depression prior to vaccination. Currently available information is insufficient to determine a causal relationship with the 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. There were no notable patterns between treatment groups for specific categories of non-serious adverse events that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Participants 16 Years of Age and Older – After Booster Dose

In Study 4, a placebo-controlled booster study, participants 16 years of age and older recruited from Study 2 received a booster dose of Pfizer-BioNTech COVID-19 Vaccine (5,081 participants), or placebo (5,044 participants) at least 6 months after the second dose of Pfizer-BioNTech COVID-19 Vaccine. Overall, participants who received a booster dose, had a median follow-up time of 2.5 months after the booster dose to the cut-off date (5 October 2021).

A higher frequency of lymphadenopathy (2.8% vs 0.4%) was observed in participants receiving a booster dose in Study 4 compared to participants receiving 2 doses.

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 from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis

Gastrointestinal Disorders: diarrhea, vomiting

Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)

Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)*

Nervous System Disorder: paresthesia, hypoesthesia

Skin and Subcutaneous Tissue Disorder: erythema multiforme

* A higher frequency of pain in extremity (1.1% vs. 0.8%) was observed in participants receiving a booster dose in Study 4 compared

to participants receiving 2 doses.

8 REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS

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

The vaccination provider enrolled in the COVID-19 Vaccination Program is responsible for MANDATORY reporting of the listed events following Pfizer-BioNTech COVID-19 Vaccine:

- 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

IMPORTANT: When reporting adverse events or vaccine administration errors to Pfizer Singapore, please provide detailed information. It is important that the information reported 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 report. Subsequent reporting of follow-up information should be completed if additional details become available.

Other Reporting Instructions

Vaccination providers may report all other adverse events, to the extent feasible, to Pfizer Singapore using the contact information below.

Email	Fax number	Telephone number
SGP.AEReporting@pfizer.com	8001012817 (local toll free)	+65 6403 8888

Adverse Event Reporting to HSA

Healthcare professionals are required to report any suspected serious adverse events observed with the use of Pfizer-BioNTech COVID-19 Vaccine to HSA as soon as possible. All fatal and life-threatening events are to be reported as soon as possible, within 24 hours. Please report the adverse events to the Vigilance and Compliance Branch at Tel: 6866 1111, Fax: 6478 9069, or report online at <https://www.hsa.gov.sg/adverse-events>.

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

Interim Authorization of Pfizer-BioNTech COVID-19 Vaccine in adolescents 12 through 18 years of age is based on safety, immunogenicity and efficacy data in this age group and in adults.

Interim 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 who received the primary series 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 Interim Authorization (18.1)*]. Of the total number of Pfizer-BioNTech COVID-19 Vaccine recipients in Study 2 as of March 13, 2021

(N = 22,026), 20.7% (n = 4,552) were 65 years of age and older and 4.2% (n = 925) were 75 years of age and older.

The safety of a booster dose of Pfizer-BioNTech COVID-19 Vaccine in individuals 65 years of age and older is based on safety data in 12 booster dose recipients 65 through 85 years of age in Study 2, 306 booster dose recipients 18 through 55 years of age in Study 2, and 1,175 booster dose recipients 65 years of age and older in Study 4. The effectiveness of a booster dose of Pfizer-BioNTech COVID-19 Vaccine in individuals 65 years of age and older is based on effectiveness data in 306 booster dose recipients 18 through 55 years of age in Study 2, and an efficacy analysis from participants 16 years of age and older in 9,945 participants in Study 4.

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 INTERIM AUTHORIZATION

18.1 Efficacy in Participants 16 Years of Age and Older – After 2 Doses

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 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. The efficacy analyses included participants that received their second

vaccination within 19 to 42 days after their first vaccination. The majority (93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1. 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 9 presents the specific demographic characteristics in the studied population.

Table 9: 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 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/m²)
- 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 10.

Table 10: 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 n^{1b} Surveillance Time^c (n^{2d})	Placebo N^a=18,325 Cases n^{1b} Surveillance Time^c (n^{2d})	Vaccine Efficacy % (95% CI)
All participants ^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
65 through 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8) ^g
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0) ^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 n^{1b} Surveillance Time^c (n^{2d})	Placebo N^a=20,172 Cases n^{1b} Surveillance Time^c (n^{2d})	Vaccine Efficacy % (95% CI)
All participants ^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
65 through 74 years	1	14	92.9

	0.424 (3239)	0.423 (3255)	(53.2, 99.8) ^g
75 years and older	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0) ^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.

- N = Number of participants in the specified group.
- n1 = Number of participants meeting the endpoint definition.
- 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.
- n2 = Number of participants at risk for the endpoint.
- No confirmed cases were identified in adolescents 12 through 15 years of age.
- Two-sided 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.
- Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Updated efficacy analyses were performed with additional confirmed COVID-19 cases accrued during blinded placebo-controlled follow-up through March 13, 2021, representing up to 6 months of follow-up after Dose 2 for participants in the efficacy population.

The updated vaccine efficacy information is presented in Table 11.

Table 11: 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 During the Placebo-Controlled Follow-up Period

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=20,998 Cases n1^b Surveillance Time^c (n2^d)	Placebo N^a=21,096 Cases n1^b Surveillance Time^c (n2^d)	Vaccine Efficacy % (95% CI^e)
All participants ^f	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
16 through 64 years	70 4.859 (15,519)	710 4.654 (15,515)	90.6 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)
65 through 74 years	6 0.994 (3350)	98 0.966 (3379)	94.1 (86.6, 97.9)
75 years and older	1 0.239 (842)	26 0.237 (847)	96.2 (76.9, 99.9)

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=22,166 Cases n1^b Surveillance Time^c (n2^d)	Placebo N^a=22,320 Cases n1^b Surveillance Time^c (n2^d)	Vaccine Efficacy % (95% CI^e)
All participants ^f	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
16 through 64 years	74 5.073 (16,218)	727 4.879 (16,269)	90.2 (87.6, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)
65 through 74 years	6 1.021 (3450)	102 0.992 (3468)	94.3 (87.1, 98.0)
75 years and older	1 0.246 (865)	26 0.240 (858)	96.2 (77.2, 99.9)

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.

- N = Number of participants in the specified group.
- n1 = Number of participants meeting the endpoint definition.
- 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.
- n2 = Number of participants at risk for the endpoint.
- Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
- Included confirmed cases in participants 12 through 15 years of age: 0 in the Pfizer-BioNTech COVID-19 Vaccine group (both without and with or without evidence of prior SARS-CoV-2 infection); 16 and 18 in the placebo group (without and with or without evidence of prior SARS-CoV-2 infection, respectively).

The updated subgroup analyses of vaccine efficacy by demographic characteristics are presented in Table 12 and Table 13.

Table 12: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 by Demographic Characteristics – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	Pfizer-BioNTech COVID-19 Vaccine N^a=20,998 Cases n1^b Surveillance Time^c (n2^d)	Placebo N^a=21,096 Cases n1^b Surveillance Time^c (n2^d)	Vaccine Efficacy % (95% CI^e)
Sex			
Male	42 3.246 (10,637)	399 3.047 (10,433)	90.1 (86.4, 93.0)
Female	35 3.001 (10,075)	451 2.956 (10,280)	92.4 (89.2, 94.7)

Subgroup	Pfizer-BioNTech COVID-19 Vaccine N^a=20,998 Cases n1^b Surveillance Time^c (n2^d)	Placebo N^a=21,096 Cases n1^b Surveillance Time^c (n2^d)	Vaccine Efficacy % (95% CI)^e
Ethnicity			
Hispanic or Latino	29 1.786 (5161)	241 1.711 (5120)	88.5 (83.0, 92.4)
Not Hispanic or Latino	47 4.429 (15,449)	609 4.259 (15,484)	92.6 (90.0, 94.6)
Race			
Black or African American	4 0.545 (1737)	48 0.527 (1737)	91.9 (78.0, 97.9)
White	67 5.208 (17,186)	747 5.026 (17,256)	91.3 (88.9, 93.4)
All others ^f	6 0.494 (1789)	55 0.451 (1720)	90.0 (76.9, 96.5)
Country			
Argentina	15 1.012 (2600)	108 0.986 (2586)	86.5 (76.7, 92.7)
Brazil	12 0.406 (1311)	80 0.374 (1293)	86.2 (74.5, 93.1)
Germany	0 0.047 (236)	1 0.048 (242)	100.0 (-3874.2, 100.0)
South Africa	0 0.080 (291)	9 0.074 (276)	100.0 (53.5, 100.0)
Turkey	0 0.027 (228)	5 0.025 (222)	100.0 (-0.1, 100.0)
United States	50 4.674 (16,046)	647 4.497 (16,094)	92.6 (90.1, 94.5)

Notes: 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).

Included confirmed cases in participants 12 through 15 years of age: 0 in the Pfizer-BioNTech COVID-19 Vaccine group; 16 in the placebo group.

* 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.

- N = Number of participants in the specified group.
- n1 = Number of participants meeting the endpoint definition.
- 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.
- n2 = Number of participants at risk for the endpoint.
- Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
- All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

Table 13: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 by Demographic Characteristics – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	Pfizer-BioNTech COVID-19 Vaccine N^a=22,166 Cases n¹^b Surveillance Time^c (n2^d)	Placebo N^a=22,320 Cases n¹^b Surveillance Time^c (n2^d)	Vaccine Efficacy % (95% CI)^e
Sex			
Male	44 3.376 (11,103)	411 3.181 (10,920)	89.9 (86.2, 92.8)
Female	37 3.133 (10,539)	462 3.093 (10,769)	92.1 (88.9, 94.5)
Ethnicity			
Hispanic or Latino	32 1.862 (5408)	245 1.794 (5391)	87.4 (81.8, 91.6)
Not Hispanic or Latino	48 4.615 (16,128)	628 4.445 (16,186)	92.6 (90.1, 94.6)
Race			
Black or African American	4 0.611 (1958)	49 0.601 (1985)	92.0 (78.1, 97.9)
White	69 5.379 (17,801)	768 5.191 (17,880)	91.3 (88.9, 93.3)
All others ^f	8 0.519 (1883)	56 0.481 (1824)	86.8 (72.1, 94.5)
Country			
Argentina	16 1.033 (2655)	110 1.017 (2670)	85.7 (75.7, 92.1)
Brazil	14 0.441 (1419)	82 0.408 (1401)	84.2 (71.9, 91.7)
Germany	0 0.047 (237)	1 0.048 (243)	100.0 (-3868.6, 100.0)
South Africa	0 0.099 (358)	10 0.096 (358)	100.0 (56.6, 100.0)
Turkey	0 0.029 (238)	6 0.026 (232)	100.0 (22.2, 100.0)
United States	51 4.861 (16,735)	664 4.678 (16,785)	92.6 (90.2, 94.6)

Notes: 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).

Included confirmed cases in participants 12 through 15 years of age: 0 in the Pfizer-BioNTech COVID-19 Vaccine group; 18 in the placebo group.

* 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.

Subgroup	Pfizer-BioNTech COVID-19 Vaccine N^a=22,166 Cases n1^b Surveillance Time^c (n2^d)	Placebo N^a=22,320 Cases n1^b Surveillance Time^c (n2^d)	Vaccine Efficacy % (95% CI)^e
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d. n2 = Number of participants at risk for the endpoint.

e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

f. All others = American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

The updated subgroup analyses of vaccine efficacy by risk status in participants are presented in Table 14 and Table 15.

Table 14: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants Without Evidence of Infection* Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	Pfizer-BioNTech COVID-19 Vaccine N^a=20,998 Cases n1^b Surveillance Time^c (n2^d)	Placebo N^a=21,096 Cases n1^b Surveillance Time^c (n2^d)	Vaccine Efficacy % (95% CI)^e
First COVID-19 occurrence from 7 days after Dose 2 ^f	77 6.247 (20,712)	850 6.003 (20,713)	91.3 (89.0, 93.2)
At risk ^g			
Yes	35 2.797 (9167)	401 2.681 (9136)	91.6 (88.2, 94.3)
No	42 3.450 (11,545)	449 3.322 (11,577)	91.0 (87.6, 93.6)
Age group (years) and risk status			
16 through 64 and not at risk	41 2.776 (8887)	385 2.661 (8886)	89.8 (85.9, 92.8)
16 through 64 and at risk	29 2.083 (6632)	325 1.993 (6629)	91.5 (87.5, 94.4)
65 and older and not at risk	1 0.553 (1870)	53 0.546 (1922)	98.1 (89.2, 100.0)
65 and older and at risk	6 0.680 (2322)	71 0.656 (2304)	91.8 (81.4, 97.1)
Obese^h			
Yes	27 2.103 (6796)	314 2.050 (6875)	91.6 (87.6, 94.6)
No	50 4.143 (13,911)	536 3.952 (13,833)	91.1 (88.1, 93.5)

Subgroup	Pfizer-BioNTech COVID-19 Vaccine N^a=20,998 Cases n^{1b} Surveillance Time^c (n^{2d})	Placebo N^a=21,096 Cases n^{1b} Surveillance Time^c (n^{2d})	Vaccine Efficacy % (95% CI)^e
Age group (years) and obesity status			
16 through 64 and not obese	46 3.178 (10,212)	444 3.028 (10,166)	90.1 (86.6, 92.9)
16 through 64 and obese	24 1.680 (5303)	266 1.624 (5344)	91.3 (86.7, 94.5)
65 and older and not obese	4 0.829 (2821)	79 0.793 (2800)	95.2 (87.1, 98.7)
65 and older and obese	3 0.404 (1370)	45 0.410 (1426)	93.2 (78.9, 98.7)

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.

- N = Number of participants in the specified group.
- n1 = Number of participants meeting the endpoint definition.
- 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.
- n2 = Number of participants at risk for the endpoint.
- Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.
- Included confirmed cases in participants 12 through 15 years of age: 0 in the Pfizer-BioNTech COVID-19 Vaccine group; 16 in the placebo group.
- At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥ 30 kg/m² or BMI $\geq 95^{\text{th}}$ percentile [12 through 15 Years of age]).
- Obese is defined as BMI ≥ 30 kg/m². For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Table 15: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Participants With or Without* Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period

Subgroup	Pfizer-BioNTech COVID-19 Vaccine N^a=22,166 Cases n^{1b} Surveillance Time^c (n^{2d})	Placebo N^a=22,320 Cases n^{1b} Surveillance Time^c (n^{2d})	Vaccine Efficacy % (95% CI)^e
First COVID-19 occurrence from 7 days after Dose 2 ^f	81 6.509 (21,642)	873 6.274 (21,689)	91.1 (88.8, 93.0)
At risk ^g			
Yes	36 2.925 (9601)	410 2.807 (9570)	91.6 (88.1, 94.2)
No	45 3.584 (12,041)	463 3.466 (12,119)	90.6 (87.2, 93.2)

Subgroup	Pfizer-BioNTech COVID-19 Vaccine N^a=22,166 Cases n1^b Surveillance Time^c (n2^d)	Placebo N^a=22,320 Cases n1^b Surveillance Time^c (n2^d)	Vaccine Efficacy % (95% CI)^e
Age group (years) and risk status			
16 through 64 and not at risk	44 2.887 (9254)	397 2.779 (9289)	89.3 (85.4, 92.4)
16 through 64 and at risk	30 2.186 (6964)	330 2.100 (6980)	91.3 (87.3, 94.2)
65 and older and not at risk	1 0.566 (1920)	55 0.559 (1966)	98.2 (89.6, 100.0)
65 and older and at risk	6 0.701 (2395)	73 0.672 (2360)	92.1 (82.0, 97.2)
Obese^h			
Yes	28 2.207 (7139)	319 2.158 (7235)	91.4 (87.4, 94.4)
No	53 4.301 (14,497)	554 4.114 (14,448)	90.8 (87.9, 93.2)
Age group (years) and obesity status			
16 through 64 and not obese	49 3.303 (10,629)	458 3.158 (10,614)	89.8 (86.2, 92.5)
16 through 64 and obese	25 1.768 (5584)	269 1.719 (5649)	91.0 (86.4, 94.3)
65 and older and not obese	4 0.850 (2899)	82 0.811 (2864)	95.3 (87.6, 98.8)
65 and older and obese	3 0.417 (1415)	46 0.420 (1462)	93.4 (79.5, 98.7)

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. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.
- f. Included confirmed cases in participants 12 through 15 years of age: 0 in the Pfizer-BioNTech COVID-19 Vaccine group; 18 in the placebo group.
- g. At risk is defined as having at least 1 of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥ 30 kg/m² or BMI $\geq 95^{\text{th}}$ percentile [12 through 15 years of age]).
- h. Obese is defined as BMI ≥ 30 kg/m². For the 12 through 15 years of age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.

Efficacy Against Severe COVID-19 – After 2 Doses

Updated efficacy analyses of secondary efficacy endpoints supported benefit of the Pfizer-BioNTech COVID-19 Vaccine in preventing severe COVID-19. Vaccine efficacy against severe COVID-19 is presented only for participants with or without prior SARS-CoV-2 infection (Table 16) as the COVID-19 case counts in participants without prior SARS-CoV-2 infection were the same as those in participants with or without prior SARS-CoV-2 infection in both the Pfizer-BioNTech COVID-19 Vaccine and placebo groups.

Table 16: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants With or Without* Prior SARS-CoV-2 Infection Based on FDA[†] or Centers for Disease Control and Prevention (CDC)[‡] Definition After Dose 1 or From 7 Days After Dose 2 in the Placebo-Controlled Follow-up

Vaccine Efficacy – First Severe COVID-19 Occurrence Based on FDA Definition			
	Pfizer-BioNTech COVID-19 Vaccine Cases n1^a Surveillance Time (n2^b)	Placebo Cases n1^a Surveillance Time (n2^b)	Vaccine Efficacy % (95% CI^c)
After Dose 1 ^d	1 8.439 ^e (22,505)	30 8.288 ^e (22,435)	96.7 (80.3, 99.9)
7 days after Dose 2 ^f	1 6.522 ^g (21,649)	21 6.404 ^g (21,730)	95.3 (70.9, 99.9)
Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC Definition			
	Pfizer-BioNTech COVID-19 Vaccine Cases n1^a Surveillance Time (n2^b)	Placebo Cases n1^a Surveillance Time (n2^b)	Vaccine Efficacy % (95% CI^c)
After Dose 1 ^d	1 8.427 ^e (22,473)	45 8.269 ^e (22,394)	97.8 (87.2, 99.9)
7 days after Dose 2 ^f	0 6.514 ^g (21,620)	32 6.391 ^g (21,693)	100 (88.0, 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.

[†] Severe illness from COVID-19 as defined by FDA is confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥ 30 breaths per minute, heart rate ≥ 125 beats per minute, saturation of oxygen $\leq 93\%$ on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen < 300 mm Hg);
- Respiratory failure [defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure < 90 mm Hg, diastolic blood pressure < 60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

[‡] Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

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

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

- c. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.
- d. Efficacy assessed based on the Dose 1 all available efficacy (modified intention-to-treat) population that included all randomized participants who received at least 1 dose of study intervention.
- e. 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 Dose 1 to the end of the surveillance period.
- f. Efficacy assessed based on the evaluable efficacy (7 Days) population that included all eligible randomized participants who receive all dose(s) of study intervention as randomized within the predefined window, have no other important protocol deviations as determined by the clinician.
- g. 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.

18.2 Efficacy in Adolescents 12 Through 15 Years of Age – After 2 Doses

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 17.

Table 17: 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.

An updated efficacy analysis of Study 2 has been performed in approximately 2,260 adolescents 12 through 15 years of age evaluating confirmed COVID-19 cases accrued up to a data cutoff date of September 2, 2021, representing up to 6 months of follow-up after Dose 2 for participants in the efficacy population.

The updated vaccine efficacy information in adolescents 12 through 15 years of age is presented in Table 18.

Table 18: 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=1057 Cases n¹^b Surveillance Time^c (n²^d)	Placebo N^a=1030 Cases n¹^b Surveillance Time^c (n²^d)	Vaccine Efficacy % (95% CI^e)
Adolescents 12 through 15 years of age	0 0.343 (1043)	28 0.322 (1019)	100.0 (86.8, 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=1109 Cases n¹^b Surveillance Time^c (n²^d)	Vaccine Efficacy % (95% CI^e)
Adolescents 12 through 15 years of age	0 0.362 (1098)	30 0.345 (1088)	100.0 (87.5, 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. Two-sided 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 – After 2 Doses

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 19).

Table 19: 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.

- n = Number of participants with valid and determinate assay results for the specified assay at the given dose/sampling time point.
- Protocol-specified timing for blood sample collection.
- 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 $0.5 \times \text{LLOQ}$.
- 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).
- Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67.
- 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 Participants 18 Years of Age and Older – After Booster Dose

Effectiveness of a booster dose of Pfizer-BioNTech COVID-19 Vaccine was demonstrated by evaluating noninferiority immune responses of SARS-CoV-2 50% neutralizing titers (NT50) 1 month after a booster dose. In Study 2, an analysis of SARS-CoV-2 NT50 demonstrated noninferior immune responses 1 month after a booster dose compared to 1 month after Dose 2 in participants at least 18 through 55 years of age who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after the booster dose, based on prespecified noninferiority criteria for both GMR and difference in seroresponse rates. Seroresponse for a participant was defined as achieving a ≥ 4 -fold rise from baseline (before Dose 1) in NT50 (Table 20 and Table 21).

The SARS-CoV-2 NT50 GMR of 1 month after the booster dose to 1 month after Dose 2 was 3.29 (2 sided 97.5% CI: 2.76, 3.91), which met the noninferiority criteria for GMR (lower bound of the 2-sided 97.5% CI > 0.67 and point estimate of the GMR ≥ 0.8).

A high proportion of participants (99.5%) had seroresponse 1 month after Dose 3 compared with 98.0% 1 month after Dose 2. The difference in proportions of participants with a seroresponse 1 month after the booster (Dose 3) and 1 month after Dose 2 (Dose 3 minus Dose 2) was 1.5% (2 sided 97.5% CI: -0.7%, 3.7%), which met the 10% noninferiority criterion (i.e., lower bound of the 2 sided 97.5% CI > -10%).

Table 20: Summary of Geometric Mean Ratio for 50% Neutralizing Titer – Comparison of 1 Month After Booster Dose to 1 Month After Dose 2 – Participants Without Evidence of Infection up to 1 Month After Booster Dose* – Booster Dose Evaluable Immunogenicity Population

Assay	n ^a	Pfizer-BioNTech COVID-19 Vaccine Sampling Time Point			Met Noninferiority Objective ^d (Y/N)
		1 Month After Booster Dose	1 Month After Dose 2	1 Month After Booster Dose - 1 Month After Dose 2	
		GMT ^b (95% CI ^b)	GMT ^b (95% CI ^b)	GMR ^c (97.5% CI ^c)	
SARS-CoV-2 neutralization assay - reference strain - NT50 (titer) ^e	210	2476.4 (2210.1, 2774.9)	753.7 (658.2, 863.1)	3.29 (2.76, 3.91)	Y

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMT = geometric mean titer; LLOQ = lower limit of quantitation; N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; Y/N = yes/no.

- * Participants who had no serological or virological evidence (up to 1 month after receipt of a booster dose of Pfizer-BioNTech COVID-19 Vaccine) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative and SARS-CoV-2 not detected by NAAT [nasal swab]) and had a negative NAAT (nasal swab) at any unscheduled visit up to 1 month after the booster dose were included in the analysis.
- a. n = Number of participants with valid and determinate assay results at both sampling time points within specified window.
- b. GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.
- c. GMRs and 2-sided 97.5% CIs were calculated by exponentiating the mean differences in the logarithms of the assay and the corresponding CIs (based on the Student t distribution).
- d. Noninferiority is declared if the lower bound of the 2-sided 97.5% CI for the GMR is > 0.67 and the point estimate of the GMR is ≥ 0.80.
- e. SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

Table 21: Percentage Difference of Participants Achieving Seroreponse – Comparison of 1 Month After Booster Dose to 1 Month After Dose 2 – Phase 3 – Participants Without Evidence of Infection up to 1 Month After Booster Dose* – Booster Dose Evaluable Immunogenicity Population

Assay	N ^a	Pfizer-BioNTech COVID-19 Vaccine Sampling Time Point		Difference (1 Month After Booster Dose - 1 Month After Dose 2) % ^d (97.5% CI ^e)	Met Noninferiority Objective ^f (Y/N)
		1 Month After Booster Dose n ^b % (95% CI ^c)	1 Month After Dose 2 n ^b % (95% CI ^c)		
		SARS-CoV-2 neutralization assay - reference strain - NT50 (titer) ^g	198	197 99.5 (97.2, 100.0)	

Abbreviations: CI = confidence interval; LLOQ = lower limit of quantitation; N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; Y/N = yes/no.

Note: Seroreponse is defined as achieving a ≥ 4 -fold rise from baseline (before Dose 1). If the baseline measurement is below the LLOQ, a postvaccination assay result $\geq 4 \times$ LLOQ is considered a seroreponse.

* Participants who had no serological or virological evidence (up to 1 month after receipt of booster dose) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative and SARS-CoV-2 not detected by NAAT [nasal swab]) and had a negative NAAT (nasal swab) at any unscheduled visit up to 1 month after booster dose were included in the analysis.

- N = number of participants with valid and determinate assay results for the specified assay at baseline, 1 month after Dose 2 and 1 month after the booster dose within specified window. These values are the denominators for the percentage calculations.
- n = Number of participants with seroreponse for the given assay at the given dose/sampling time point.
- Exact 2-sided CI based on the Clopper and Pearson method.
- Difference in proportions, expressed as a percentage (1 month after booster dose – 1 month after Dose 2).
- Adjusted Wald 2-sided CI for the difference in proportions, expressed as a percentage.
- Noninferiority is declared if the lower bound of the 2-sided 97.5% CI for the percentage difference is $> -10\%$.
- SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

18.5 Relative Vaccine Efficacy in Participants 16 Years of Age and Older – After Booster Dose

An interim efficacy analysis of Study 4, a placebo-controlled booster study, was performed in approximately 10,000 participants 16 years of age and older who were recruited from Study 2, evaluated confirmed COVID-19 cases accrued from at least 7 days after booster vaccination up to a data cut-off date of 5 October 2021, which represents a median of 2.5 months post-booster follow-up. Vaccine efficacy of the Pfizer-BioNTech COVID-19 Vaccine booster dose after the primary series relative to the placebo booster group who only received the primary series dose was assessed. The relative vaccine efficacy information for participants 16 years of age and older is presented in Table 22.

Table 22: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Booster Vaccination – Participants 16 Years of Age and Older Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Booster Vaccination – Evaluable Efficacy Population

First COVID-19 occurrence from 7 days after booster dose in participants without evidence of prior SARS-CoV-2 infection*			
	Pfizer-BioNTech COVID-19 Vaccine N^a=4695 Cases n¹^b Surveillance Time^c (n²^d)	Placebo N^a=4671 Cases n¹^b Surveillance Time^c (n²^d)	Relative Vaccine Efficacy^e % (95% CI^f)
First COVID-19 occurrence from 7 days after booster vaccination	6 0.823 (4659)	123 0.792 (4614)	95.3 (89.5, 98.3)
First COVID-19 occurrence from 7 days after booster dose in participants with or without evidence of prior SARS-CoV-2 infection			
	Pfizer-BioNTech COVID-19 Vaccine N^a=4993 Cases n¹^b Surveillance Time^c (n²^d)	Placebo N^a=4952 Cases n¹^b Surveillance Time^c (n²^d)	Relative Vaccine Efficacy^e % (95% CI^f)
First COVID-19 occurrence from 7 days after booster vaccination	7 0.871 (4934)	124 0.835 (4863)	94.6 (88.5, 97.9)

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 serological or virological evidence (prior to 7 days after receipt of the booster vaccination) 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 Visit 1, and had a negative NAAT [nasal swab] at any unscheduled visit prior to 7 days after booster vaccination) were included in the analysis.

- N = Number of participants in the specified group.
- n1 = Number of participants meeting the endpoint definition.
- 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 the booster vaccination to the end of the surveillance period.
- n2 = Number of participants at risk for the endpoint.
- Relative vaccine efficacy of the Pfizer-BioNTech COVID-19 Vaccine booster group relative to the placebo group (non-booster).
- Two-sided confidence interval (CI) for relative vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

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 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 -90°C to -60°C (-130°F to -76°F) 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 February 2022 through December 2022 printed on the label may remain in use beyond the printed date until the updated expiry date shown below; as long as approved storage conditions between -90°C to -60°C (-130°F to -76°F) have been maintained.

<u>Printed Expiry Date</u>		<u>Updated Expiry Date</u>
02/2022	→	31-Aug-2022
03/2022	→	30-Sep-2022
06/2022	→	30-Sep-2022
07/2022	→	31-Oct-2022
08/2022	→	30-Nov-2022
09/2022	→	31-Dec-2022
10/2022	→	31-Jan-2023
11/2022	→	28-Feb-2023
12/2022	→	31-Mar-2023

If not stored between -90°C to -60°C (-130°F to -76°F), 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 -90°C to -60°C (-130°F to -76°F); not exceeding the expiry date (EXP). 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 -90°C to -60°C (-130°F to -76°F). 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 -90°C to -60°C (-130°F to -76°F); not exceeding the expiry date (EXP).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2°C to 8°C (35°F to 46°F)] for up to 31 days; not exceeding the expiry date (EXP). 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 25°C (77°F)] 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 48 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 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
<p data-bbox="310 1528 594 1558">www.cvdvaccine.com</p> 	<p data-bbox="1068 1625 1263 1654">+65 6403 8888</p>

For medical information enquires, please submit your medical information enquires at <https://pmiform.com/HCP/SG>.

Alternatively, you may send them to MedicalInformationSingapore@pfizer.com.

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

BIONTECH

Manufactured for
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Manufactured by
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Reference label: CDS version 12.0

Revised: 03 August 2022