Clinical Study Results

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study vaccine works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor:	BioNTech SE
Sponsor Agent:	Pfizer Inc.
Vaccine Studied:	Comirnaty® (Pfizer-BioNTech RNA-based COVID-19 Vaccine), also known as BNT162b2
Protocol Number:	C4591048 Substudy B
Dates of Study:	23 September 2022 to 19 January 2024
Title of this Study:	A Study to Learn About Bivalent COVID-19 RNA Vaccine Candidate(s) in Healthy Children (Substudy B) [A Master Phase 1/2/3 Protocol to Investigate the Safety, Tolerability, and Immunogenicity of Variant-Adapted BNT162b2 RNA-Based Vaccine Candidate(s) in Healthy Children]
Date of this Report:	15 August 2024

– Thank You –

If you and your child participated in this study, Pfizer, the Sponsor Agent, would like to thank you for your participation.

This summary will describe the study results. If you or your child have any questions about the study or the results, please contact the doctor or staff at your child's study site.

Why was this study done?

What is COVID-19?

Coronavirus disease 2019 (or COVID-19) is caused by a virus called **s**evere **a**cute **r**espiratory **s**yndrome **co**rona**v**irus **2** (SARS-CoV-2).

COVID-19 spreads easily from person to person and can cause mild to severe illness. People with COVID-19 can have fever, chills, cough, loss of taste or smell, or trouble breathing.

All viruses, including the COVID-19 virus, are expected to change over time. These changes or mutations from the original virus are called different strains or **"variants"**. Compared to the original COVID-19 virus, the **Omicron** strain spreads more easily between people.

What is BNT162b2 vaccine?

BNT162b2 (also known as Comirnaty®) is an injectable vaccine that may help the body's immune system to defend against COVID-19.

- It does not contain a whole virus or any part of the virus that can cause COVID-19.
- It is made up of a part of the virus's genetic code, surrounded by fatty particles called lipids. It uses the body's own cells to produce a spike protein, which may help the body produce antibodies to fight against COVID-19.

BNT162b2 is the original monovalent COVID-19 vaccine. A monovalent vaccine is designed to protect against 1 strain of a virus. BNT162b2 was designed to protect against the **original strain** of the COVID-19 virus. BNT162b2 is called **Original BNT** in this report.

In this study, participants received a different form of BNT162b2, which was designed to protect against both the **original** and the **Omicron BA.4/BA.5** strains of the COVID-19 virus. This is called **Bivalent BNT** in this report. A bivalent vaccine is designed to protect against 2 different strains of a virus.

While the study was ongoing, health agencies in the United States (US) and other countries have authorized or approved Bivalent BNT for use in children 6 months and older. After Bivalent BNT was authorized for use, researchers had difficulty finding people who wanted to enroll in a bivalent COVID-19 vaccine study.

Enrollment in this study was stopped because of health agencies' recommendations to change the strain composition of COVID-19 vaccines to a monovalent Omicron XBB.1.5. After enrollment in this study had stopped, a total of 1398 participants had already signed up to join this study.

What was the purpose of this study?

This study wanted to learn if healthy children developed immune responses against the COVID-19 virus after getting Bivalent BNT.

When a person first gets a vaccine, a protective **immune response** is triggered in the body. This means that the body's immune system is activated to make **antibodies**.

- **Antibodies** are proteins that can fight off infections and help prevent disease.
- An **immune response** is the body's ability to find and fight off germs that cause disease.

This study also wanted to learn if Bivalent BNT is safe for healthy children.

- Throughout the study, researchers checked how participants were feeling.
- Researchers also checked if participants had local reactions or systemic symptoms after their Bivalent BNT shot in this study.

Local reactions include the following:

- For participants **6 months to under 2 years old**, any tenderness, redness, or swelling at the injection site (thigh).
- For participants **2 years to under 5 years old**, any pain, redness, or swelling at the injection site (arm).

Systemic symptoms include the following:

- For participants **6 months to under 2 years old**, any fever, loss of appetite, sleepiness, or irritability.
- For participants **2 years to under 5 years old**, any fever, tiredness, headache, chills, vomiting, diarrhea, muscle pain, or joint pain.

Researchers wanted to know:

- **Did participants have immune responses to Omicron BA.4/BA.5 strain of the COVID-19 virus after vaccination with Bivalent BNT?**
- **How many participants had local reactions or systemic symptoms within 7 days after vaccination with Bivalent BNT?**
- **How many participants had a medical problem within 1 month after each vaccination with Bivalent BNT?**
- **How many participants had a serious medical problem within 6 months after the last vaccination with Bivalent BNT?**

What happened during the study?

How was the study done?

Participants were divided into 3 groups. Table 1 and Figure 1 below show the vaccinations that each group received before joining this study and those they received in this study. All participants were to receive Bivalent BNT 3 micrograms (mcg) in this study.

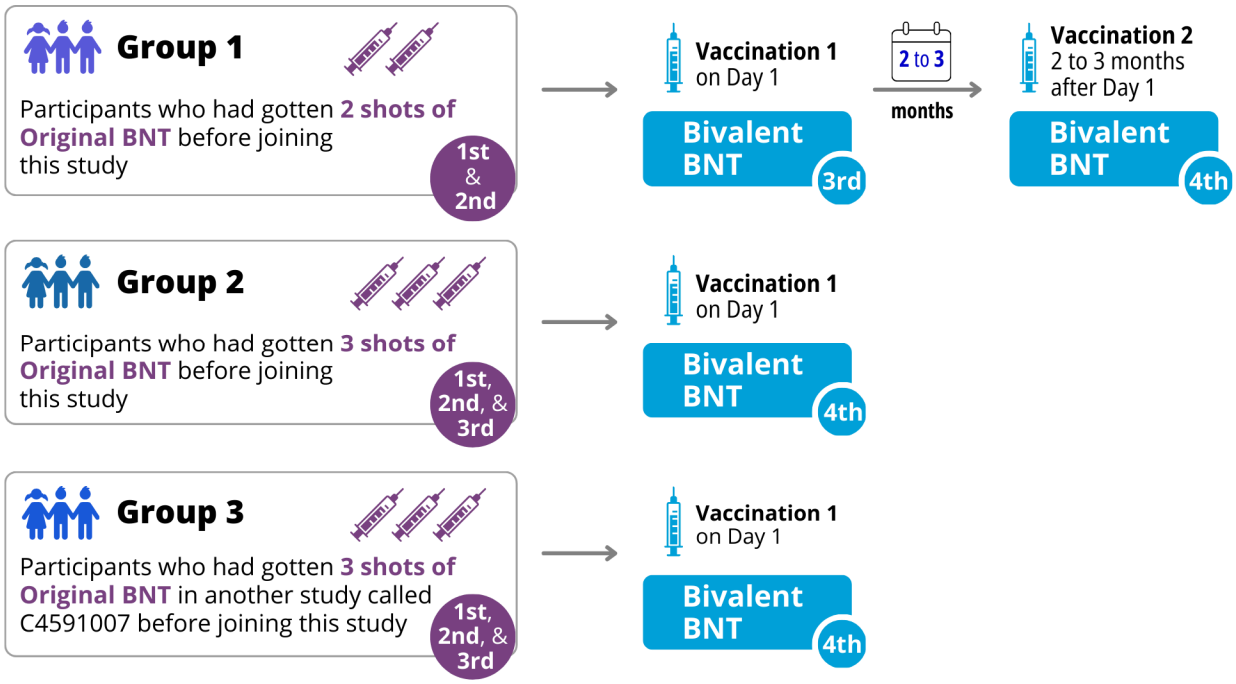
Table 1. The 3 groups in this study

Group	Vaccinations Before Joining This Study	Vaccinations in This Study
Group 1: age 6 months to under 4 years and 6 months	Participants had 2 shots of **Original BNT** before joining this study, with their 2nd dose given 2 to 5 months before joining this study.	They got 2 shots of **Bivalent BNT** in this study as **Vaccinations 1 and 2** (given 2 to 3 months apart), which were their 3rd and 4th doses of the COVID-19 vaccine.
Group 2: age 6 months to under 5 years	Participants had 3 shots of **Original BNT** before joining this study, with their 3rd dose given 2 to 8 months before joining this study.	They got 1 shot of **Bivalent BNT** in this study as **Vaccination 1**, which was their 4th dose of the COVID-19 vaccine.
Group 3: age 6 months to under 5 years	Participants had 3 shots of **Original BNT** in another study called **C4591007** before joining this study, with their 3rd dose given at least 2 months before joining this study.	They got 1 shot of **Bivalent BNT** in this study as **Vaccination 1**, which was their 4th dose of the COVID-19 vaccine.

This was an "open-label study". This means that the participants' parents/guardians, researchers, and staff knew that participants got Bivalent BNT in this study.

Figure 1 below shows what happened in the study.

Figure 1. What happened during the study?



Participants had health checks done through 6 months after their last vaccination. They also had blood samples taken at scheduled visits.

Where did this study take place?

This study ran at 19 locations for Group 2 participants and 46 locations for Groups 1 and 3 participants in the US.

When did this study take place?

It began on 23 September 2022 and ended on 19 January 2024.

Who participated in this study?

The study included healthy children 6 months to under 5 years old. As shown in Table 1 and Figure 1 above, participants must have received 2 or 3 shots of Original BNT before joining this study.

Across the 3 groups, participants were between 9 months and 4 years old.

A total of 1398 participants started this study. Table 2 below shows how many participants in each group took part in the study.

Table 2. Number of participants who took part in the study

	Group 1	Group 2	Group 3
Started the study	31 participants	310 participants	1057 participants
Got the study vaccine	30 of 31 participants (96.8%) got Vaccination 1. Out of the 30 participants, there were 18 boys (60.0%) and 12 girls (40.0%). 29 of 31 participants (93.5%) got Vaccination 2.	All 310 participants (100%) got the study vaccine. Out of the 310 participants, there were 156 boys (50.3%) and 154 girls (49.7%).	All 1057 participants (100%) got the study vaccine. Out of the 1057 participants, there were 515 boys (48.7%) and 542 girls (51.3%).
Did not get the study vaccine	1 of 31 participants (3.2%) did not get Vaccination 1.	None	None
Finished the study	28 of 31 participants (90.3%)	299 of 310 participants (96.5%)	1036 of 1057 participants (98.0%)
Did not finish the study	2 of 31 participants (6.5%)	11 of 310 participants (3.5%)	21 of 1057 participants (2.0%)

Among the participants in the 3 groups that did not finish the study (Table 2), the most common reasons were either:

- Their parents/guardians decided for the participants to stop taking part in the study.
- Their parents/guardians could not be contacted for the participants' check-up.

How long did the study last?

Each participant was in the study for about 6 to 9 months. The entire study took 16 months to complete.

The Sponsor Agent began reviewing the information collected while the study was ongoing. The Sponsor Agent created reports of the results after each review. When the study ended in January 2024, the Sponsor Agent reviewed the information that was not reported before. The Sponsor Agent then created a report of the results. This is a summary of that report.

What were the results of the study?

Did participants have immune responses to Omicron BA.4/BA.5 strain of the COVID-19 virus after vaccination with Bivalent BNT?

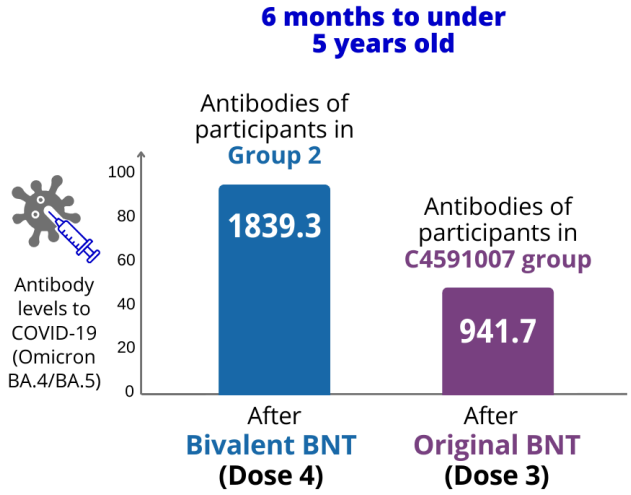
Researchers wanted to find out if participants in **Group 2** had immune responses to **Omicron BA.4/BA.5 strain** of the COVID-19 virus after their **Bivalent BNT** shot in this study. To find out:

- Researchers measured the participants' **antibody levels** to Omicron BA.4/BA.5 strain of the COVID-19 virus **before** vaccination and 1 month **after** vaccination in this study.
- Antibody levels can tell us about the body's immune response (ability to find and fight off germs that cause disease).

Researchers then compared the results of **Group 2** participants after their **Bivalent BNT** shot (4th dose of COVID-19 vaccine) with the results of a group of participants in another study called **C4591007** after their **Original BNT** shot (3rd dose of COVID-19 vaccine). This group of participants was of the same age group as the Group 2 participants.

Figure 2 below shows the results.

Figure 2. What were the participants' antibody levels to Omicron BA.4/BA.5 of the COVID-19 virus at 1 month after vaccination?



At 1 month after vaccination:

Group 2 participants who got **Bivalent BNT** (4th dose) had about **2 times more** antibodies to Omicron BA.4/BA.5 of the COVID-19 virus than the participants from the **C4591007** group who got **Original BNT** (3rd dose).

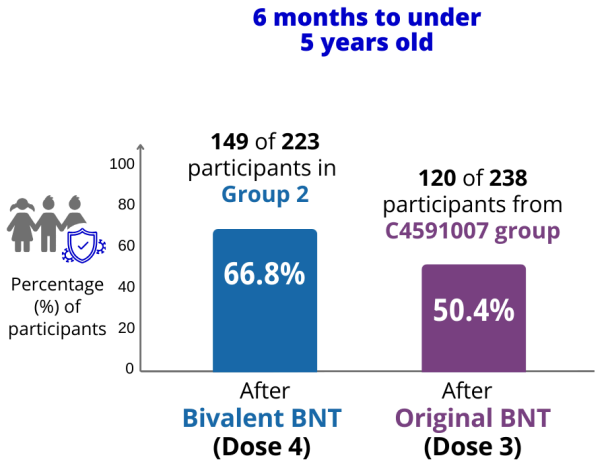
Researchers found that these results are likely not due to chance. This means that **Bivalent BNT** given as the 4th dose may produce more antibodies to help protect healthy children 6 months to under 5 years old against Omicron BA.4/BA.5 of the COVID-19 virus better than the **Original BNT** given as the 3rd dose.

Researchers also wanted to find out how many participants in **Group 2** had **strong immune responses** to Omicron BA.4/BA.5 strain of the COVID-19 virus after their **Bivalent BNT** shot in this study.

- In this study, a strong immune response means the antibody levels were at least **4 times higher** at 1 month **after** vaccination compared to **before** vaccination.
- This can tell us how many children made a lot of antibodies after vaccination in this study.

Figure 3 below shows the results. A total of 223 participants in Group 2 and 238 participants from the C4591007 group had available results at 1 month after vaccination.

Figure 3. How many participants had strong immune responses to Omicron BA.4/BA.5 of the COVID-19 virus at 1 month after vaccination?



At 1 month after vaccination:

The percentage of participants with strong immune responses to Omicron BA.4/BA.5 of the COVID-19 virus was comparable between **Group 2** who got **Bivalent BNT** (4th dose) and the **C4591007** group who got **Original BNT** (3rd dose).

Researchers found that these results are likely not due to chance. This means that **Bivalent BNT** given as the 4th dose may help healthy children 6 months to under 5 years old produce a strong immune response to Omicron BA.4/BA.5 of the COVID-19 virus as well as the **Original BNT** given as the 3rd dose.

Overall, study results of Group 2 participants showed that **Bivalent BNT** given as the 4th dose may help protect children 6 months to under 5 years old against COVID-19 infection caused by Omicron BA.4/BA.5 strain.

How many participants had local reactions or systemic symptoms within 7 days after vaccination with Bivalent BNT?

The parents or guardians recorded in an electronic diary if their children (participants) had any local reactions or systemic symptoms within 7 days after their Bivalent BNT shot.

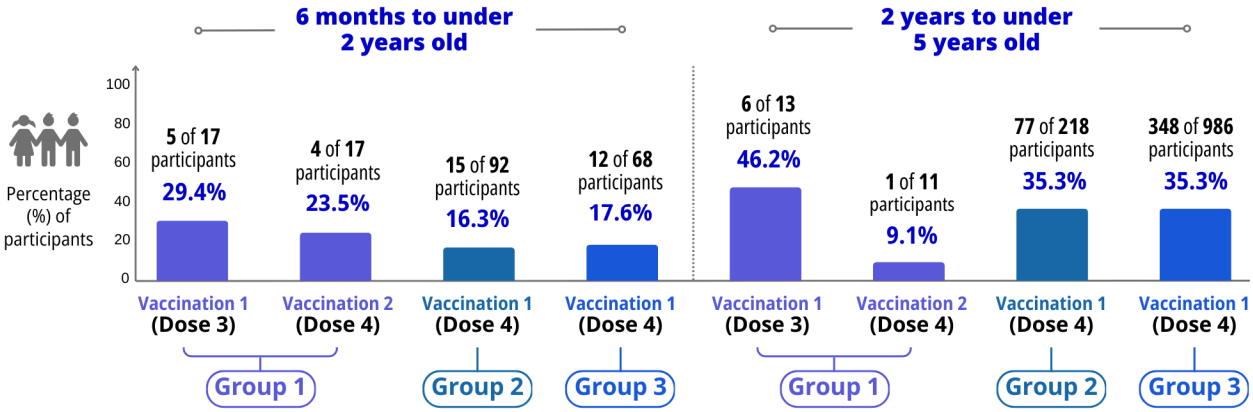
Local reactions

In this study, local reactions include the following:

- For participants **6 months to under 2 years old**, any tenderness, redness, or swelling at the injection site (thigh).
- For participants **2 years to under 5 years old**, any pain, redness, or swelling at the injection site (arm).

Figure 4 below shows how many participants had local reactions within 7 days after their Bivalent BNT shot.

Figure 4. How many participants had local reactions within 7 days after vaccination with Bivalent BNT?



Across the 3 vaccine groups:

- Most of the injection site reactions were mild or moderate in severity and lasted about 1 to 8 days.
- The most common local reactions were:
  - **Injection site tenderness** in participants 6 months to under 2 years old.
  - **Injection site pain** in participants 2 years to under 5 years old.

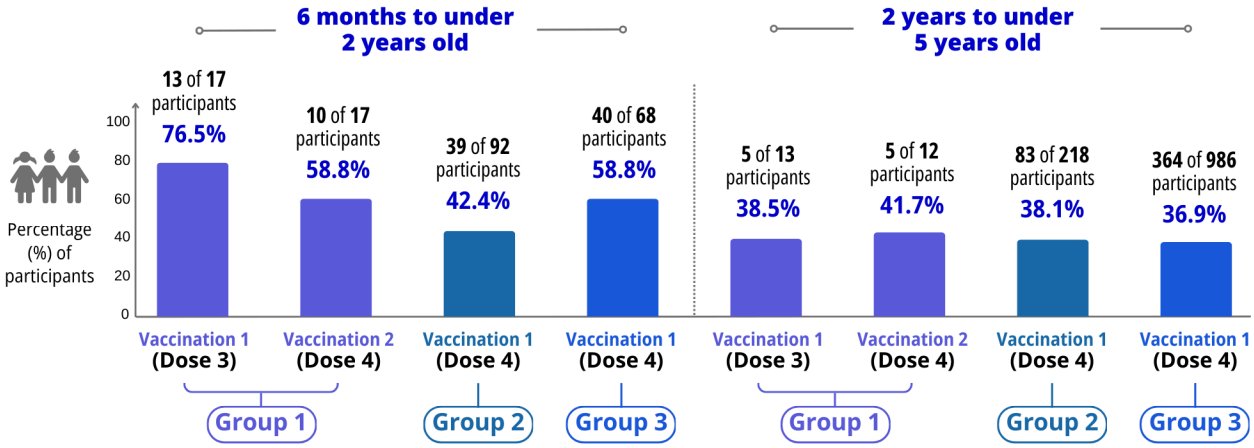
Systemic symptoms

In this study, systemic symptoms include the following:

- For participants **6 months to under 2 years old**, any fever, loss of appetite, sleepiness, or irritability.
- For participants **2 years to under 5 years old**, any fever, tiredness, headache, chills, vomiting, diarrhea, muscle pain, or joint pain.

Figure 5 below shows how many participants had systemic symptoms within 7 days after their Bivalent BNT shot.

Figure 5. How many participants had systemic symptoms within 7 days after vaccination with Bivalent BNT?



Across the 3 vaccine groups:

- Most of the systemic symptoms were mild or moderate in severity and lasted about 1 to 5 days.
- The most common systemic symptoms were:
    - **Irritability** in participants 6 months to under 2 years old.
    - **Tiredness** in participants 2 years to under 5 years old.

This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study. Other studies may have different results.

What medical problems did participants have during the study?

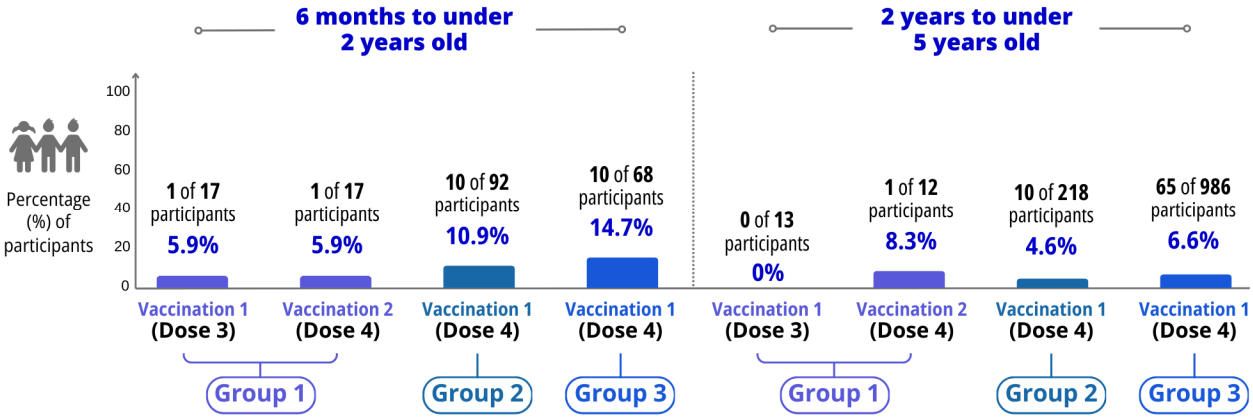
The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study vaccine or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many vaccine groups in many studies, doctors try to understand what effects a study vaccine might have on a participant.

The parents or guardians reported any medical problems their children (participants) had during this study.

How many participants had a medical problem within 1 month after each vaccination with Bivalent BNT?

Figure 6 below shows how many participants had at least 1 medical problem within 1 month after each vaccination with Bivalent BNT.

Figure 6. How many participants had medical problems within 1 month after each vaccination with Bivalent BNT?



No participant in any of the 3 vaccine groups left the study because of medical problems they experienced during the study.

The most common medical problems within 1 month after each vaccination with Bivalent BNT – seen in at least 5 participants in any of the 3 vaccine groups – were fever and vomiting. The list below shows how many participants had fever or vomiting.

Fever:

- **Group 1:** 1 out of 30 participants (**3.3%**) had fever within 1 month after Vaccination 1. This participant was 6 months to under 2 years old. None of the 29 participants (**0%**) had fever within 1 month after Vaccination 2.
- **Group 2:** 4 out of 310 participants (**1.3%**) had fever within 1 month after vaccination. Of these participants, 1 was 6 months to under 2 years old, and 3 were 2 years to under 5 years old.
- **Group 3:** 10 out of 1057 participants (**0.9**%) had fever within 1 month after vaccination. Of these participants, 2 were 6 months to under 2 years old, and 8 were 2 years to under 5 years old.

Vomiting:

- **Group 1:** None of the 30 participants (**0%**) had vomiting within 1 month after Vaccination 1. None of the 29 participants (**0%**) had vomiting within 1 month after Vaccination 2.
- **Group 2:** 3 out of 310 participants (**1.0%**) had vomiting within 1 month after vaccination. Of these participants, 2 were 6 months to under 2 years old, and 1 was 2 years to under 5 years old.
- **Group 3:** 11 out of 1057 participants (**1.0%**) had vomiting within 1 month after vaccination. Of these participants, 3 were 6 months to under 2 years old, and 8 were 2 years to under 5 years old.

Did study participants have any serious medical problems?

A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems.

How many participants had a serious medical problem within 6 months after the last vaccination with Bivalent BNT?

- **Group 1:** None of the 30 participants had serious medical problems from Vaccination 1 through 6 months after Vaccination 2.
- **Group 2:** 1 out of 310 participants (**0.3%**) had a serious medical problem within 6 months after vaccination. The serious medical problem was a breathing-related sleep disorder.
- **Group 3:** 11 out of 1057 participants (**1.0%**) had serious medical problems within 6 months after vaccination. The most common serious medical problem within 6 months after vaccination – seen in at least 2 participants in **Group 3** – was asthma. Overall, 2 out of 1057 participants (**0.2%**) had asthma.

The participants in Groups 2 and 3 who had serious medical problems were **2 years to under 5 years old**. No participant 6 months to under 2 years old had serious medical problems within 6 months after vaccination.

Researchers do not believe any of the reported serious medical problems were caused by the study vaccine. No participant in any of the 3 vaccine groups died during the study.

Where can I learn more about this study?

If you or your child have questions about the results of your study, please speak with the doctor or staff at your child's study site.

For more details on your study protocol, please visit:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **C4591048 Substudy B**

The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier **NCT05543616**

Please remember that researchers look at the results of many studies to find out which vaccines can work and are safe for patients.

Again, if you and your child participated in this study, **thank you** for volunteering.
We do research to try to find the best ways to help patients, and you helped us to do that!