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 medication 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: Pfizer Inc.

Vaccine Studied: *Clostridioides difficile* Vaccine (PF-06425090)

Protocol Number: B5091007

Dates of Study: 29 March 2017 to 21 December 2021

Title of this Study: *Clostridium Difficile* Vaccine Efficacy Trial (Clover)
[A Phase 3, Placebo-Controlled, Randomized, Observer-Blinded Study to Evaluate the Efficacy, Safety, and Tolerability of a *Clostridium Difficile* Vaccine in Adults 50 Years of Age and Older]

Date(s) of this Report: 18 November 2022

– Thank You –

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

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

Why was this study done?

What is *Cloistridioides difficile* infection?

Cloistridioides difficile (previously called *Clostridium difficile* and also known as *C. difficile)* is a germ or bacteria that can be found in the bowel of some people.

C. difficile infections can range from a person not showing any symptoms or having mild diarrhea, to more serious complications such as severe diarrhea and life-threatening damage to the bowel.

C. difficile infection mostly affects people who have recently been treated with antibiotics, have had to stay in a healthcare setting (such as a hospital or nursing home) for a long time, are over 65 years old, or have a weakened "immune system" because of other illnesses. The immune system is what defends the body from germs like *C. difficile.*

What is *C. difficile* vaccine (PF-06425090)?

Vaccines work by helping the body to fight infections and prevent diseases. The *C. difficile* vaccine used in this study (PF-06425090) is an investigational vaccine which means it has not been approved for general use. There are currently no approved vaccines to prevent *C. difficile* infection.

In this study, the *C. difficile* vaccine was given as 3 doses of 200 micrograms each. Each dose was given by injection into a muscle. Previous studies have already shown that PF-06425090 can produce an immune system response against *C. difficile* in humans when given as 3 doses at dose levels up to 200 micrograms.

What was the purpose of this study?

There were 2 main purposes for this study. One purpose was to learn about the safety of the *C. difficile* vaccine. The second purpose was to see if the *C. difficile* vaccine helped to prevent *C. difficile* infection in adults aged 50 years and older.

Researchers wanted to know:

1. **Did the *C. difficile* vaccine help to reduce the number of new episodes of *C. difficile* infection?**
2. **How many participants had redness, swelling, or pain at the injection site within 7 days of vaccination or placebo injection?**
3. **How many participants had fever, tiredness, headache, vomiting, muscle pain, or joint pain within 7 days of vaccination or placebo injection?**
4. **How many participants had medical problems during the study?**

What happened during the study?

How was the study done?

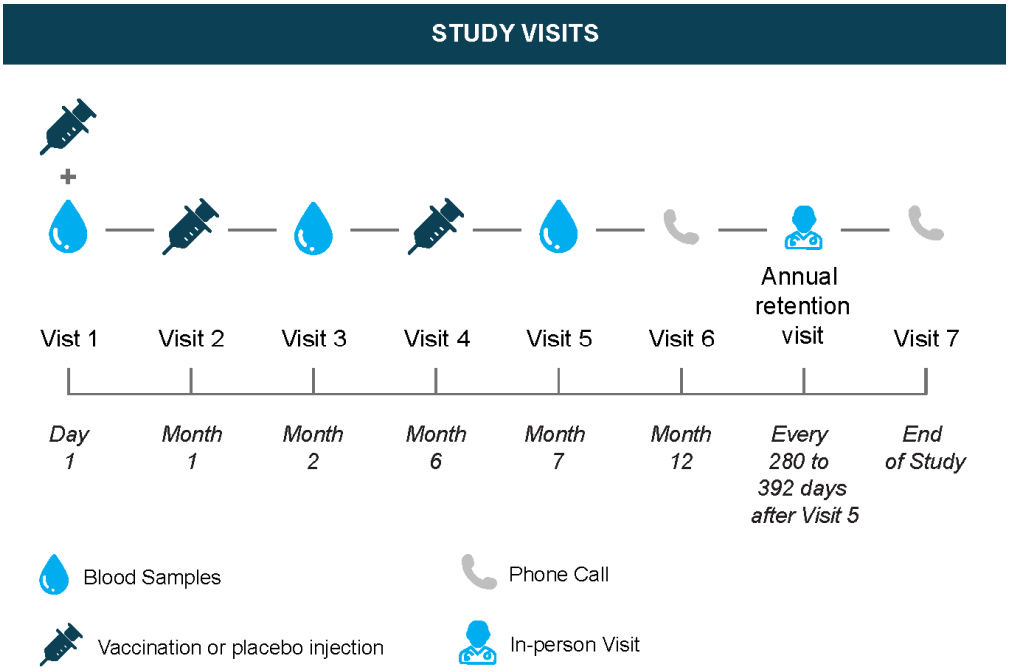
This study compared 2 groups of participants to find out if people given the *C. difficile* vaccine reacted differently compared to people given a placebo (saline injection). A placebo does not have any medicine in it but looks just like the medicine being tested.

The study participants and researchers did not know who received the *C. difficile* vaccine and who received placebo. This is known as a "blinded" study. Study participants were assigned to each group by chance alone. This is known as a "randomized" study. This is done to make the groups similar, which then makes comparing the results between the groups more fair.

A total of 17,535 participants joined the study; 8766 were assigned to the *C. difficile* vaccine group and 8769 participants were assigned to the placebo group.

The figure below shows what happened during the study.

Figure 1. What happened during the study?



The first injection of *C. difficile* vaccine or placebo was given at Day 1 (Dose 1). The second injection was given at Month 1 (Dose 2) and the third injection was given at Month 6 (Dose 3). If a participant had diarrhea 3 or more times in a 24-hour period at any time during the study, the participant collected a stool sample for testing and an in-person visit was triggered. A blood sample was taken at this additional visit.

In this study, researchers looked at the number of new *C. difficile* infections starting at 14 days after Dose 2 and starting at 14 days after Dose 3. A "new" infection meant the participant had no episodes of *C. difficile* infection in the past. A *C. difficile* infection was defined as either:

- Diarrhea 3 or more times in a 24-hour period plus a stool sample testing positive for *C. difficile*; or
- Inflammation of the bowel diagnosed by a doctor to be caused by *C. difficile* plus a stool sample testing positive for *C. difficile*

Where did this study take place?

The Sponsor ran this study at 410 locations in 23 countries in 5 regions in the world (East-Asia, Europe, North America, Oceania and South America).

When did this study take place?

It began 29 March 2017 and ended 21 December 2021.

Who participated in this study?

The study included 17,535 men and women who were at least 50 years old and who were at risk of developing a *C. difficile* infection.

- A total of 8467 men (49%) were given *C. difficile* vaccine or placebo
- A total of 8973 women (51%) were given *C. difficile* vaccine or placebo
- All participants were between the ages of 50 and 97

A total of 95% of participants received Dose 2, and 90% of participants received Dose 3. A total of 36% of participants left before the study was over. The most common reasons for leaving the study early were the participant's choice (24% of participants), lost to follow-up (4% of participants), or the participant passed away for any reason (4% of participants). Lost to follow-up means that the participant did not return for study visits and did not respond to phone calls from the study site staff.

How long did the study last?

Study participants were in the vaccination phase of the study for up to 6 months. The entire study, from the time of consent to the last follow-up, took about 4 years and 8 months to complete.

When the study ended in December 2021, the Sponsor reviewed the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

Did the *C. difficile* vaccine help to reduce the number of new episodes of *C. difficile* infection?

The number of new episodes of *C. difficile* infection measured after Dose 2 or after Dose 3 of the *C. difficile* vaccine or placebo are shown in **Figure 2** and **Figure 3**.

Figure 2. Number of new episodes of *C. difficile* infection after Dose 2

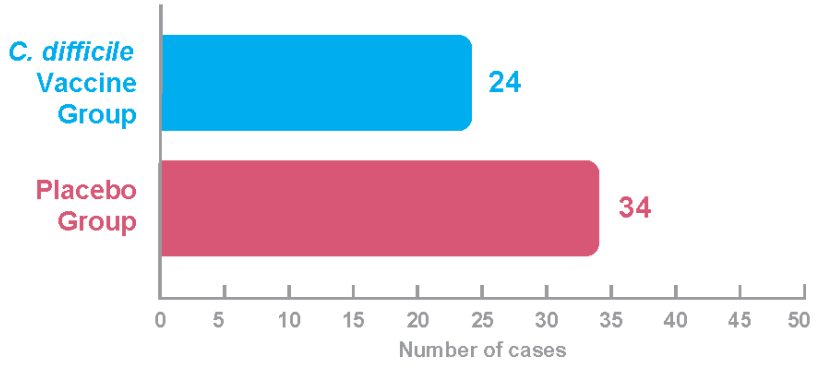
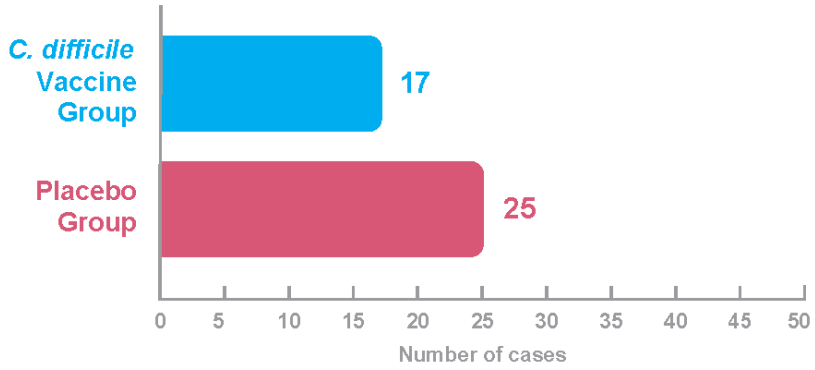


Figure 3. Number of new episodes of *C. difficile* infection after Dose 3



In this study, the *C. difficile* vaccine was 29% effective at preventing new episodes of *C. difficile* infection starting at 14 days after Dose 2. The *C. difficile* vaccine was 31% effective at preventing new episodes of *C. difficile* infection starting at 14 days after Dose 3.

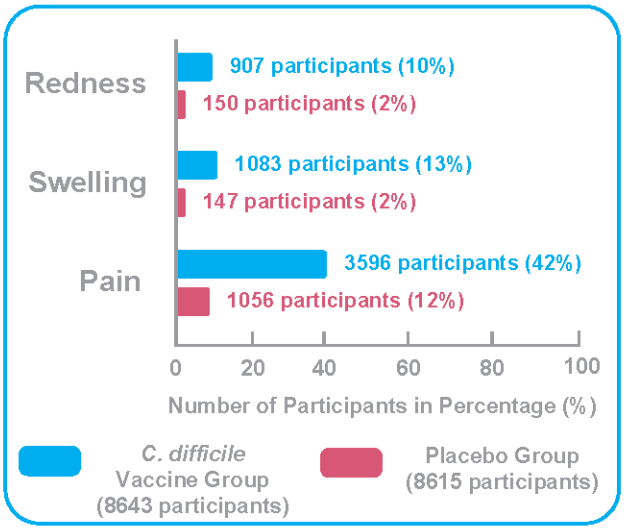
The researchers have decided that these results may be the result of chance. This means the study results did not show that the *C. difficile* vaccine was better than placebo at preventing new episodes of *C. difficile* infection.

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.

How many participants had redness, swelling, or pain at the injection site within 7 days of vaccination or placebo injection?

The graphs in **Figure 4** show the percentage of participants in each group with any redness, swelling, or pain at the injection site within 7 days after getting any dose (Dose 1, 2, or 3) of *C. difficile* vaccine or placebo. Most participants reported these effects were mild or moderate.

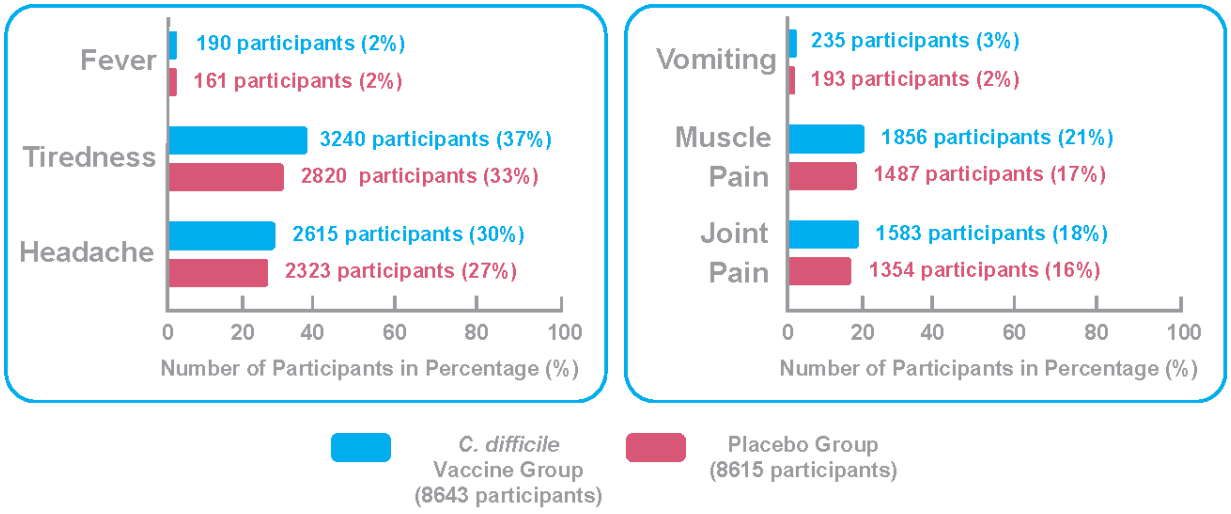
Figure 4. Percentage of participants with redness, swelling, or pain at the injection site within 7 days after any dose



How many participants had fever, tiredness, headache, vomiting, muscle pain, or joint pain within 7 days of vaccination or placebo injection?

The graphs in **Figure 5** show the percentage of participants in each group with any fever, tiredness, headache, vomiting, muscle pain, or joint pain within 7 days after getting any dose (Dose 1, 2, or 3) of *C. difficile* vaccine or placebo. Most participants reported these events were mild or moderate.

Figure 5. Percentage of participants with fever, tiredness, headache, vomiting, muscle pain, or joint pain within 7 days after any dose



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 treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medication might have on a participant.

From Dose 1 up to 1 month after Dose 3, 8211 participants (47%) in this study had at least 1 medical problem. This included 4161 participants (48%) in the *C. difficile* vaccine group, and 4050 participants (46%) in the placebo group.

A total of 543 participants (3%) left the study because of medical problems, including 291 participants (3%) in the *C. difficile* vaccine group and 252 participants (3%) in the placebo group.

The table below describes the most common medical problems – those reported by at least 1% of participants in any group from Dose 1 up to 1 month after Dose 3.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study from Dose 1 up to 1 month after Dose 3. All medical problems reported by at least 1% of participants in any group are listed.
- The **2nd** column tells how many of the 8722 participants given the *C. difficile* vaccine reported each medical problem. Next to this number

is the percentage of the 8722 participants given the *C. difficile* vaccine who reported the medical problem.

- The **3rd** column tells how many of the 8718 participants given placebo reported each medical problem. Next to this number is the percentage of the 8718 participants given placebo who reported the medical problem.
- Using these instructions, you can see that 269 out of the 8722 (3%) participants given the *C. difficile* vaccine reported a fall. A total of 292 out of the 8718 (3%) participants given placebo reported a fall.

Table 1. Most common medical problems in the study

Medical Problem	*C. Difficile* Vaccine (8722 Participants)	Placebo (8718 Participants)
Fall	269 out of 8722 participants (3%)	292 out of 8718 participants (3%)
Join pain	253 out of 8722 participants (3%)	256 out of 8718 participants (3%)
Infection of nose, sinuses, throat, voice box or windpipe	245 out of 8722 participants (3%)	237 out of 8718 participants (3%)
Infection of kidneys, bladder, or urethra	242 out of 8722 participants (3%)	226 out of 8718 participants (3%)

Infection of nose and throat (common cold)	229 out of 8722 participants (3%)	193 out of 8718 participants (2%)
Infection of larger airways into the lungs (bronchitis)	193 out of 8722 participants (2%)	183 out of 8718 participants (2%)
Back pain	151 out of 8722 participants (2%)	138 out of 8718 participants (2%)
Cough	127 out of 8722 participants (1%)	133 out of 8718 participants (2%)
Arm or leg pain	123 out of 8722 participants (1%)	101 out of 8718 participants (1%)
Lung disease	121 out of 8722 participants (1%)	109 out of 8718 participants (1%)
Swelling of the tissues in the sinuses	106 out of 8722 participants (1%)	118 out of 8718 participants (1%)
Flu (influenza)	97 out of 8722 participants (1%)	91 out of 8718 participants (1%)
Joint disease (osteoarthritis)	93 out of 8722 participants (1%)	110 out of 8718 participants (1%)
Lung infection	93 out of 8722 participants (1%)	99 out of 8718 participants (1%)

Diarrhea	92 out of 8722 participants (1%)	119 out of 8718 participants (1%)
Feeling like about to vomit (nausea)	91 out of 8722 participants (1%)	83 out of 8718 participants (1%)
Bacterial infection in the deep layers of skin (cellulitis)	85 out of 8722 participants (1%)	80 out of 8718 participants (1%)
High blood pressure	84 out of 8722 participants (1%)	103 out of 8718 participants (1%)
Headache	81 out of 8722 participants (1%)	96 out of 8718 participants (1%)

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.

A total of 2206 participants (13%, or 2206 out of 17,440 participants) had serious medical problems from Dose 1 up to 6 months after Dose 3. This included 1116 participants (13%) in the *C. difficile* vaccine group and 1090 participants (13%) in the placebo group. Most of the serious medical problems were not thought to be related to taking the study vaccine.

Lung infection was the most common serious medical problem. This happened in 70 participants in the *C. difficile* vaccine group and in 63 participants in the placebo group (less than 1% of participants).

Researchers believe that 6 participants (less than 0.1%) in the *C. difficile* vaccine group and 1 participant (less than 0.1%) in the placebo group had serious medical problems that were related to the study vaccine. None of the "related" serious medical problems were reported in more than 1 participant each.

A total of 731 participants (4%, or 731 out of 17,440 participants) died during the study. This included 369 participants (4%) in the *C. difficile* vaccine group and 362 participants (4%) in the placebo group.

Where can I learn more about this study?

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

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

www.clinicaltrials.gov	Use the study identifier **NCT03090191**
www.clinicaltrialsregister.eu	Use the study identifier **2016-003866-14**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **B5091007**

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

Again, if you 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!