CLINICAL TRIAL 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 medicine 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.

Medicine(s) Studied: *Clostridium difficile* Vaccine (PF-06425090)

Protocol Number: B5091009

Dates of Trial: 16 July 2015 to 07 March 2017

Title of this Trial: A Study Investigating the Safety of a *Clostridium difficile* Vaccine in Subjects 65 to 85 Years of Age [A Phase 2, Placebo-Controlled, Randomized, Observer-Blinded Study to Evaluate the Safety, Tolerability, and Immunogenicity of Two 3-Dose Regimens of a *Clostridium difficile* Vaccine in Health Adults Aged 65 to 85 Years]

Date of this Report: 07 January 2019

– Thank You –

Pfizer, the Sponsor, would like to thank you for your participation in this clinical trial and provide you a summary of results representing everyone who participated. If you have any questions about the study or results, please contact the doctor or staff at your study site.

WHY WAS THIS STUDY DONE?

Cloistridioides difficile (previously *Clostridium difficile*) is a germ or bacteria that can be found in the bowel of some people. This germ is also known as *C. difficile* or *C. diff*. Sometimes when people take "antibiotics" to treat an illness, the *C. difficile* that is in their bowel can multiply. This is because antibiotics kill both good and bad bacteria and killing the good bacteria gives the *C. difficile* room to spread. *C. difficile* infections are often seen in people who have a weakened "immune system" because of other illnesses or due to old age. The immune system is what defends the body from germs like *C. difficile*.

When someone has a *C. difficile* infection they will usually have diarrhea or loose stools. This is because when *C. difficile* multiples in the bowel, it can produce "toxins". A toxin is a substance made by a living cell that is harmful to the body. *C. difficile* makes 2 different toxins and these are called A and B. These toxins damage the bowel and this is what makes people ill. Doctors will prescribe antibiotics to try to get rid of *C. difficile*. For some people, the antibiotics may not work and a different antibiotic may need to be given. Sometimes these antibiotics may not work and the *C. difficile* cannot be gotten rid of easily and other treatment options are needed. If the infection cannot be treated, the diarrhea can get worse, and the person could become very ill and may die.

Researchers did this study to see if the *C. difficile* vaccine could help the body's immune system produce "antibodies" against the toxins made by *C. difficile*. Antibodies are special proteins made by the body that can recognize and help kill germs or toxins. Antibodies can protect people from getting sick if they come into contact with a germ or toxin that the body recognizes. The researchers conducting this study wanted to see if the *C. difficile* vaccine was safe and if antibodies could be made against the modified *C. difficile* toxins in the vaccine.

WHAT HAPPENED DURING THE STUDY?

This study compared 6 groups of participants to find out if people given an injection of 2 different doses of the *C. difficile* vaccine at different times reacted differently compared to people given placebo (see Table). In this study, the *C. difficile* vaccine was given at a dose of 100 micrograms or 200 micrograms, and the placebo was "saline" (also known as salt water). A placebo does not have any medicine in it, but looks similar to the medicine. Researchers use a placebo to see if the medicine they are testing worked better or was safer compared with placebo. The injections were given on Day 1, Day 8, and Day 30 in the Day Group or on Day 1, Month 1, and

Month 6 in the Month Group. Day 1 was the day that the first injection was given for both groups.

Description of Treatment Groups

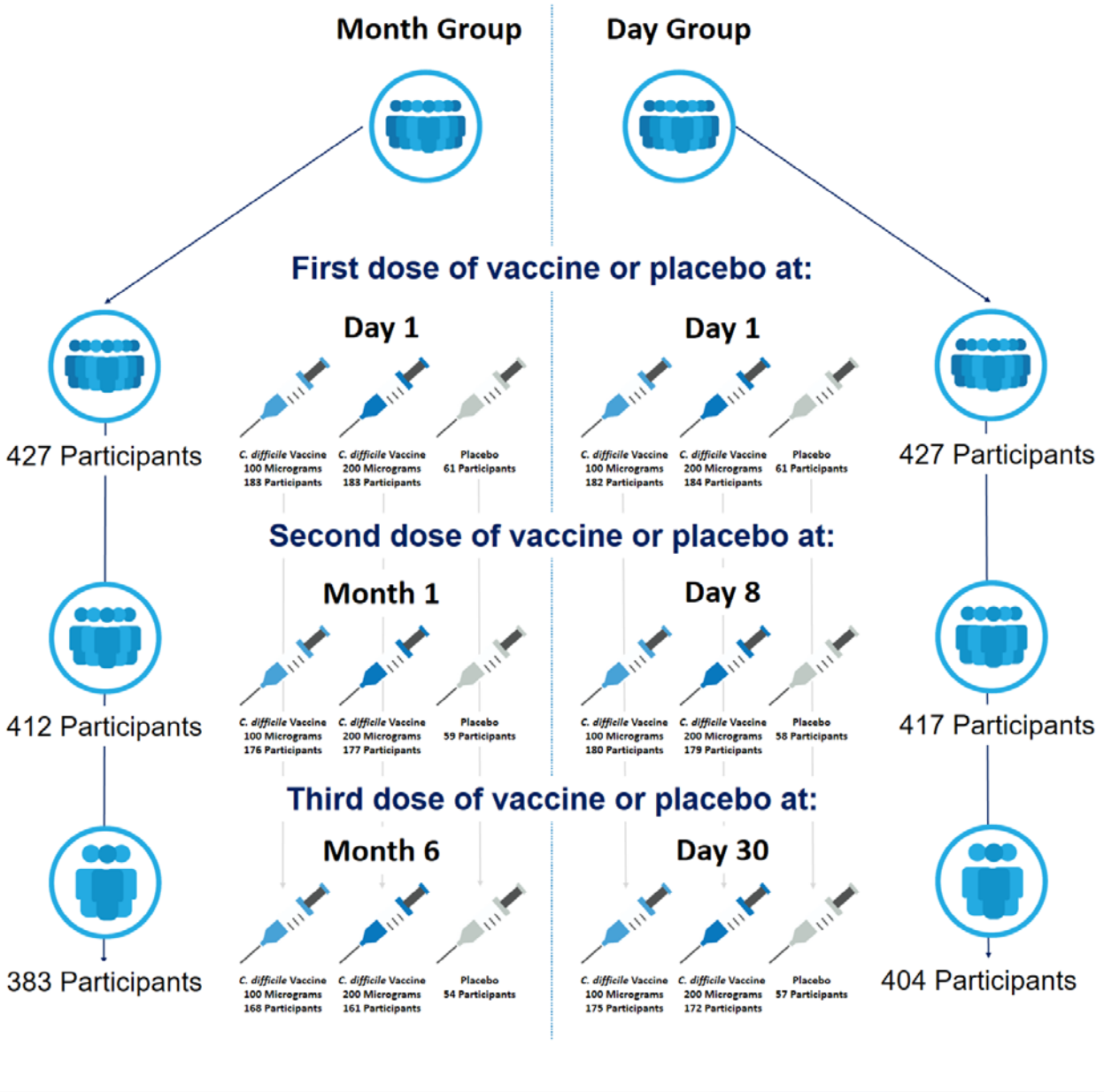
Group	Dose	Timing of the Injections
1	*C. difficile* vaccine 100 micrograms	Day Group: Injections were given on Day 1, Day 8, and Day 30
2	*C. difficile* vaccine 200 micrograms	
3	Placebo	
4	*C. difficile* vaccine 100 micrograms	Month Group: Injections were given on Day 1, Month 1, and Month 6
5	*C. difficile* vaccine 200 micrograms	
6	Placebo	

The study included participants who were healthy and 65 to 85 years of age. The participants and most of the researchers did not know who received an injection of the *C. difficile* vaccine and who received placebo. This is known as a "blinded" study. The only person who knew what injection a participant was given was the person who gave the injection. Volunteers were assigned to each group by chance alone. Participants were put into 1 of the 6 treatment groups as shown in the table above. 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.

At the end of the original study, participants who received all 3 doses of the *C. difficile* vaccine were able to enter an "extension" study and receive a fourth dose of vaccine or placebo. This new study continued after the original study ended.

While participants were only in the original study for 18 months if given the *C. difficile* vaccine in the Month Group or 13 months if given the *C. difficile* vaccine in the Day Group, the original study took almost 20 months to complete. The sponsor ran this study at 15 locations in the United States. It began on 16 July 2015 and ended on 07 March 2017. A total of 393 men and 461 women participated. All participants were between the ages of 65 and 85 years.

Of the 854 participants who started the study, 787 received all 3 doses of *C. difficile* vaccine or placebo and 740 finished the original study. In the Month Group, 427 participants (200 men and 227 women) received at least 1 dose, 412 (97%) received at least 2 doses, and 383 (90%) received all 3 doses. In the Day Group, 427 participants (193 men and 234 women) received at least 1 dose, 417 (97%) received at least 2 doses, and 404 (94%) received all 3 doses. A total of 114 participants left before the study was over by their choice or a doctor decided it was best for the participant to stop the study.



As of 21 June 2017 (the data cutoff date for the original study), the Sponsor began reviewing information collected. The Sponsor then created a report of the results. This is a summary of that report.

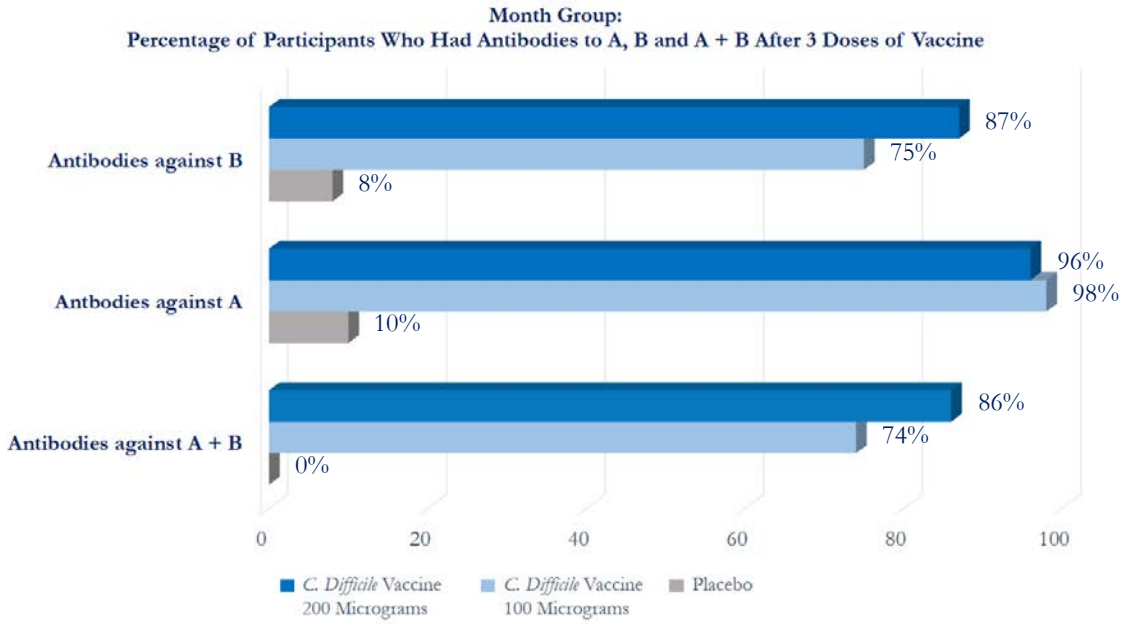
WHAT WERE THE RESULTS OF THE STUDY?

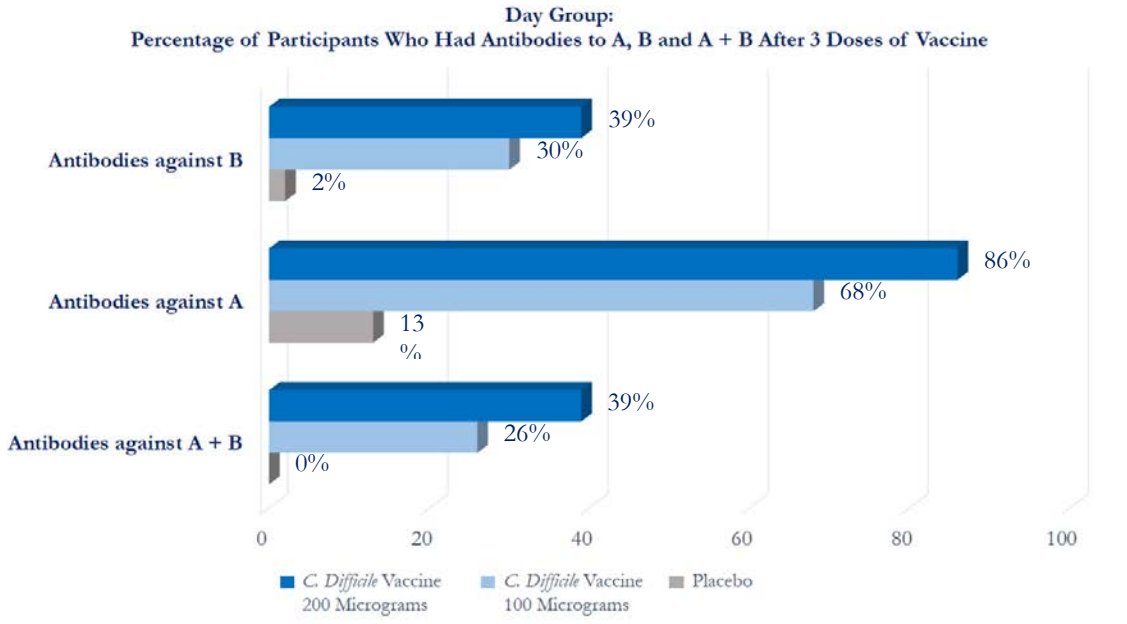
Were participants able to make antibodies when given the *C. difficile* vaccine?

The *C. difficile* vaccine contains 2 different types of protein that participants could make antibodies against. These proteins, A and B, are like the toxins produced by *C. difficile* that make people ill. The proteins in the vaccine have been changed so that they are not poisonous and won't make people sick. The researchers looked to see if participants had antibodies against A, against B, or against A and B in their blood after they had received all 3 doses. If the participants had antibodies against A, B, or A + B, then the immune system may have been able to recognize the A toxin, the B toxin, or both the A and B toxins. If the immune system could recognize these toxins then the body might have been able to get rid of the toxins before they did any harm. If antibodies against A, B or A + B were present in participants who were given placebo then this means the participant may have been exposed previously to *C. difficile* bacteria, possibly without ever knowing.

At Month 7, 1 month after the third dose of vaccine in participants in the Month Group, 160 out of 163 participants (98%) given the 100 micrograms dose and 151 out of 158 participants (96%) given the 200 micrograms dose had antibodies against A compared with 1 out of 53 participants (2%) given placebo. Antibodies against B were found in 122 out of 163 participants (75%) given the 100 micrograms dose and in 138 out of 158 participants (87%) given the 200 micrograms dose compared with 4 out of 53 participants (8%) given placebo. Antibodies against A + B were found in 121 out of 163 participants (74%) given the 100 micrograms dose and in 136 out of 158 participants (86%) given the 200 micrograms dose compared with none of the 53 participants given placebo.

At Day 37, 7 days after the third dose of vaccine in participants in the Day Group, 117 out of 171 participants (68%) given the 100 micrograms dose and 141 out of 165 participants (86%) given the 200 micrograms dose had antibodies against A compared with 7 out of 56 participants (13%) given placebo. Antibodies against B were seen in 51 out of 171 participants (30%) given the 100 micrograms dose and in 64 out of 165 participants (39%) given the 200 micrograms dose compared with 1 out of 56 participants (2%) given placebo. Antibodies against A + B were seen in 45 out of 171 participants (26%) given the 100 micrograms dose and in 64 out of 165 participants (39%) given the 200 micrograms dose compared with none of the 56 participants given placebo.





Based on these results, the researchers decided that the results were not due to chance. *C. difficile* vaccine given at a dose of either 100 micrograms or 200 micrograms in the Month Group or in the Day Group may have helped people 65 to 85 years of age develop antibodies against the modified toxins within the *C. difficile* vaccine. This vaccine may be an option for people 65 to 85 years of age who could become very ill because of *C. difficile*.

This does not mean that everyone in this study had these results. Other studies may produce different results, as well. These are just some of the main findings of the study, and more information may be available at the websites listed at the end of this summary.

Did participants who were given the *C. difficile* vaccine have any reactions to the vaccine?

The researchers looked at whether there were any "local" reactions to the vaccine. A local reaction is something that is seen at the site where the injection of the vaccine was given and can include pain at the injection site, redness, and/or swelling. Participants were asked to record details of any local reactions they had in a study diary they were given. In the Month Group, this information was collected for 14 days after each dose of vaccine. Participants in the Day Group were also asked to record this information, but this was for 7 days after dose 1 and for 14 days after dose 2 and dose 3.

In participants in the Month Group, local reactions were seen in 21% to 29% of participants given the *C. difficile* vaccine compared with 2% to 8% given placebo. In participants in the Day Group, local reactions were seen in 16% to 45% of participants given the *C. difficile* vaccine compared with 2% to 7% given placebo. Local reactions seen after the *C. difficile* vaccine were similar to the reactions seen when people are given other adult vaccines.

Month Group: Local Reactions in Participants Given Vaccine

Local Reaction Seen After	*C. difficile* Vaccine 100 Micrograms	*C. difficile* Vaccine 200 Micrograms	Placebo
Dose 1	46/182 (25%)	39/182 (21%)	5/61 (8%)
Dose 2	50/176 (28%)	52/177 (29%)	3/59 (5%)
Dose 3	40/168 (24%)	47/161 (29%)	1/54 (2%)

Day Group: Local Reactions in Participants Given Vaccine			
Local Reaction Seen After	***C. difficile* Vaccine 100 Micrograms**	***C. difficile* Vaccine 200 Micrograms**	**Placebo**
Dose 1	**36/179 (20%)**	**30/183 (16%)**	**4/61 (7%)**
Dose 2	**59/180 (33%)**	**80/179 (45%)**	**1/58 (2%)**
Dose 3	**43/175 (25%)**	**42/171 (25%)**	**2/57 (4%)**

The researchers also looked at whether there were any "systemic events" or reactions to the vaccine. Systemic means something that affects the whole body or specific parts of it like the head or joints. Systemic events were reactions that participants may have had after they had been given the vaccine, like feeling tired, muscle pain, headache, loose stools, high temperature, and/or being sick. Participants were asked to record details of any systemic events in their study diary. In the Month Group, this information was collected for 14 days after each dose of vaccine. Participants in the Day Group were also asked to record this information, but this was for 7 days after dose 1 and for 14 days after dose 2 and dose 3.

In participants in the Month Group, systemic events were seen in 31% to 50% of participants given the *C. difficile* vaccine compared with 30% to 53% given placebo. In participants in the Day Group, systemic events were seen in 18% to 37% of participants given the *C. difficile* vaccine compared with 25% to 31% given placebo. The systemic events reported after the *C. difficile* vaccine were similar to the systemic events seen when people are given other adult vaccines.

Month Group: Systemic Events in Participants Given Vaccine			
Systemic Event Seen After	***C. difficile* Vaccine 100 Micrograms**	***C. difficile* Vaccine 200 Micrograms**	**Placebo**
Dose 1	**90/182 (50%)**	**77/182 (42%)**	**32/61 (53%)**
Dose 2	**75/176 (43%)**	**65/177 (37%)**	**22/59 (37%)**
Dose 3	**62/168 (37%)**	**50/161 (31%)**	**16/54 (30%)**

Day Group: Systemic Events in Participants Given Vaccine			
Systemic Events Seen After	***C. difficile* Vaccine 100 Micrograms**	***C. difficile* Vaccine 200 Micrograms**	**Placebo**
Dose 1	**41/179 (23%)**	**55/183 (30%)**	**19/61 (31%)**
Dose 2	**55/180 (31%)**	**66/179 (37%)**	**17/58 (29%)**
Dose 3	**31/175 (18%)**	**50/171 (29%)**	**14/57 (25%)**

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 the side effects of an experimental drug or vaccine might be.

In participants given the *C. difficile* vaccine or placebo in the Month Group, 84% or 154 out of 183 participants in the 100 micrograms dose group and 84% or 153 out of 183 participants in the 200 micrograms dose group had non-serious medical problems compared with 85% or 52 out of 61 participants in the placebo group. There were very few non-serious medical problems that were reported by 2 or more participants. Most of these non-serious medical problems were each reported by 1 or 2 participants. In participants given the *C. difficile* vaccine or placebo in the Day Group, 67% or 122 out of 182 participants in the 100 micrograms dose group and 75% or 138 out of 184 participants in the 200 micrograms dose group had non-serious medical problems compared with 62% or 38 out of 61 participants in the placebo group. There were very few non-serious medical problems that were reported by 2 or more participants.

Most of these non-serious medical problems were each reported by 1 or 2 participants. A total of 16 participants left the study because of medical problems that the doctors thought were unrelated to the vaccine.

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

In the Month Group, 43 participants (10%, or 43 out of 427 participants) had serious medical problems. This included 19 participants (10%, or 19 out of 183 participants) in the *C. difficile* vaccine 100 micrograms dose group, 22 participants (12%, or 22 out of 183 participants) in the *C. difficile* 200 micrograms dose group, and 2 participants (3%, or 2 out of 61 participants) in the placebo group. In the Day Group, 17 participants (4%, or 17 out of 427 participants) had serious medical problems. This included 11 participants (6%, or 11 out of 182 participants) in the *C. difficile* vaccine 100 micrograms dose group and 6 participants (3%, or 6 out of 184 participants) in the *C. difficile* 200 micrograms dose group. None of the 61 participants in the placebo group had serious medical problems.

Overall, 5 out of the 854 participants died during the study (1%, or 5 out of 854 participants), with 2 deaths in participants in the Month Group and 3 deaths in participants in the Day Group. After review by the researchers, there were no serious medical problems or deaths that were thought to be related to the vaccine.

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 **NCT02561195**

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

Again, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!