

Developing A New Flu Prevention Drug

Part A: FLUSTOP in the News

Base your answers to questions 1-5 on the news article below. *Note: FLUSTOP is a fictitious drug, not a real drug.*

New Drug in the Fight Against the Flu

Scientists announced the discovery of FLUSTOP, an antiviral drug that prevents influenza (the flu). The antiviral drug prevents the reproduction of the influenza virus that causes the flu.

Scientists administered a FLUSTOP pill to an experimental group of 20 monkeys each day for 5 days. For a comparison, a control group of 20 other monkeys was given a placebo pill (a pill that did not contain FLUSTOP) for 5 days. Both groups of monkeys were then exposed to the influenza virus that causes the flu.

Tests of mucus collected from the monkeys' noses three days later revealed that 90% of the monkeys who received a placebo had influenza viruses in their nasal mucus. Only 10% of the monkeys who were treated with FLUSTOP had influenza viruses in their nasal mucus after three days.

In the future, FLUSTOP may be used in people to stop the influenza virus before it causes flu symptoms. Scientists caution, however, that further testing is needed to provide evidence that FLUSTOP is both safe and effective for use by humans.

1. Describe the experimental group for the scientists' experiment.

2. Describe the control group for the scientists' experiment.

3. Explain why it is important to include a control group in a well-designed experiment?

4. A placebo is fake medication that looks like the real medication but does not contain any substance likely to have an effect.

a) What is the placebo given to the control group of monkeys?

b) Explain the purpose of the placebo that was given to the control group of monkeys.

5. Explain why scientists test FLUSTOP on animals before they test it on humans.

Part B: Phase 1 Clinical Trials

Before FLUSTOP can be sold to humans, it must be scientifically tested to determine if it is safe and effective for use by humans. Human testing begins with **Phase 1 clinical trials** that are conducted to determine the dose of the FLUSTOP that is safe for humans. This testing is done with healthy volunteers who do not have flu symptoms.

Thirty healthy human volunteers signed informed consent forms indicating that they understood the risks involved in participating as research subjects. These volunteers were paid for participating in the research.

Informed consent is a process for getting permission before enrolling a participant in a clinical trial. An informed consent form includes a discussion of:

- What will happen to participants during a clinical trial.
- The risks, benefits, and uncertainties related to participation in the clinical trial.
- Participation in the clinical trial is voluntary.

1. What is the purpose of the informed consent form that the human volunteers signed?

2. Add 1 drop of “FLUSTOP—10 mg per drop” to the Human Volunteer 1 cup. Stir with a clean plastic toothpick for 5 seconds. Observe the color.
 - A colorless solution indicates that the volunteer is healthy.
 - A pink or red color indicates that an unsafe amount of FLUSTOP has been given to the volunteer.
3. Repeat step 2 and count the number of drops that need to be added to turn the color of the fluid in the cup to pink or red color. Be sure to add 1 drop at a time and stir for 5 seconds between adding drops.
4. Use the data table below to record the number of drops needed to change the color of fluid in the Volunteer 1 cup from colorless (safe) to pink or red (unsafe).

Human Volunteer #	Drops of FLUSTOP needed to turn fluid to pink or red	Highest dose (drops) of FLUSTOP that is safe for this volunteer	Highest dose (milligrams) of FLUSTOP that is safe for this volunteer. (1 drop = 10 mg)
1			
2			
3			

5. Repeat steps 2-4 using the Human Volunteer 2 and Human Volunteer 3 cups. Be sure to use a new toothpick for each volunteer.
6. Complete the data table on the previous page by writing the highest dose (milligrams) of FLUSTOP that is safe for each volunteer. Hint: 1 drop contains 10 milligrams of FLUSTOP.
7. Which human volunteer is most sensitive to the harmful effects of FLUSTOP? _____
8. Explain why it was not appropriate to use the average milligrams of FLUSTOP to determine the safe level of FLUSTOP that should be used for further human testing.

9. From the results of the Phase 1 clinical trials, what is the highest dose of FLUSTOP that could safely be used for further human testing? Remember that each drop contains 10 mg of FLUSTOP. Express your answer in milligrams (mg). _____
10. Explain why it was important to test the FLUSTOP on more than one volunteer.

11. **Summarize:** Explain the purpose for Phase 1 Clinical Trials.

12. **Cleanup:** Discard used toothpicks. Empty the cups with Volunteer solutions into the sink and then discard these cups. Rinse and dry the measuring cup and dropper then return them to your teacher.

Part C: Phase 2 Clinical Trials

A **Phase 2 clinical trial** is a scientific experiment used to determine if a drug is safe and effective for use by humans. For the FLUSTOP Phase 2 clinical trial, 200 people who had not had the flu or a flu vaccination were recruited as research subjects.

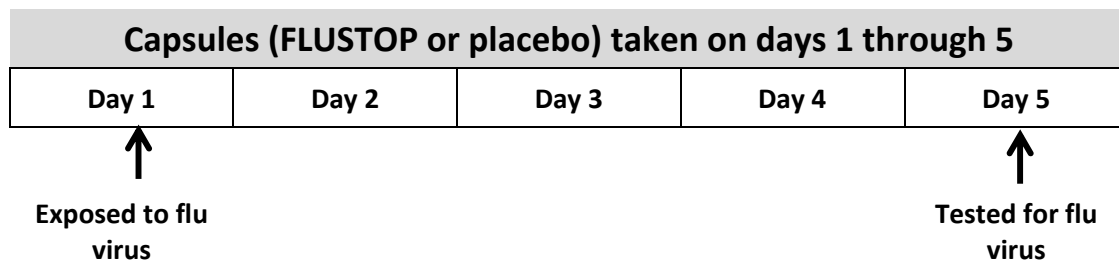
The research subjects were randomly assigned to either the experimental group (100 subjects) or the control group (100 subjects). **Random assignment** is used to create experimental and control groups that are approximately the same at the beginning of an experiment. The procedure involves flipping a coin to determine whether a subject is assigned to the experimental or control group.

1. What is the purpose for a Phase 2 clinical trial?

2. Why is it important that the researchers randomly assign research subjects to the experimental group or control group?

Members of both the experimental group and the control group were exposed to the influenza virus on day 1. Because the subjects might experience mild to serious flu symptoms or transmit the flu virus to their families or friends, the research subjects were confined to a hospital isolation setting for five days after exposure to the flu virus.

Members of the experimental group each took one 60 mg capsule of FLUSTOP on days 1 through 5. Members of the control group each took one placebo capsule on days 1 through 5. The placebo capsule looked like FLUSTOP, but only contained inactive ingredients.



3. An informed consent form was used to make sure that research subjects understand the potential risks of participating in the Phase 2 clinical trial. List at least two things that should be included on the informed consent form for the Phase 2 clinical trial.

- _____
- _____

4. How were the experimental group and the control group different?

5. How were the experimental group and the control group the same?

On day 5, the researchers tested all of the research subjects to see if they had influenza viruses that had reproduced. The researchers used cotton swabs to collect mucus from the noses of all research subjects. Each cotton swab was then tested for influenza virus.

You will conduct tests to determine if the mucus samples collected from some of the research subjects contain influenza viruses. You will test the mucus samples from 5 research subjects in the experimental group and 5 research subjects in the control group.

6. Use a measuring cup or graduated cylinder to add 20 mL of tap water to each of the bags labeled "For Influenza Tests." These bags contain a small amount of test powder.
7. Close the bags completely and gently swirl the contents of the bag for approximately 1 minute
8. Open one of the bags and place the **Experimental Group Influenza Test Sheet** into it. Completely seal the bag so it does not leak. Lay the bag flat on your desk.
9. Open the other bag and place the **Control Group Influenza Test Sheet** into it. Completely seal the bag so it does not leak. Lay the bag flat on your desk.
10. Observe the circles on both the experimental group and control group test sheets.
 - Pink circles on the test sheets represent people who have the influenza virus in their nasal mucus.
 - White circles represent people who do not have the influenza virus in their nasal mucus.

11. Complete the data table below for the experimental group and the control group.

- Record the number of white circles and pink circles.
- Calculate the percentage of people who have influenza viruses in their nasal mucus.

Group	White Circles (do <u>not</u> have influenza viruses)	Pink Circles (have influenza viruses)	Total Circles	Percentage of people who have influenza viruses in their nasal mucus
Experimental (FLUSTOP)			5	
Control (placebo)			5	

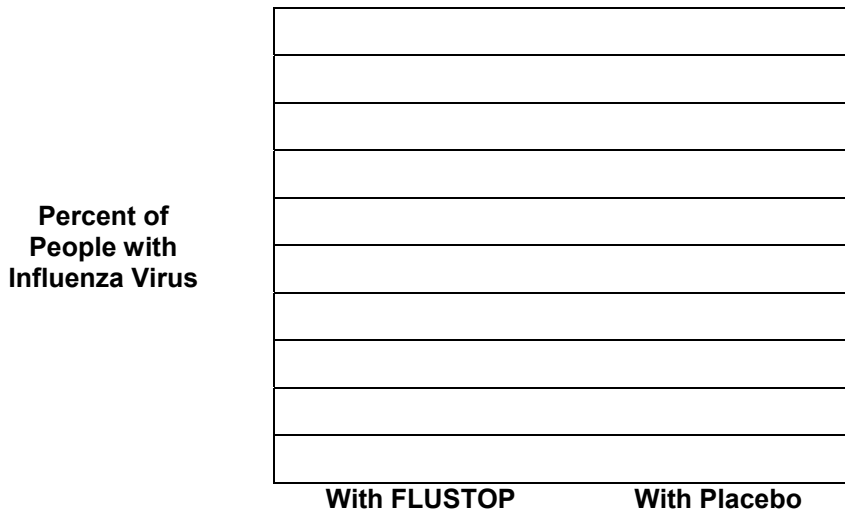
12. **Cleanup:** Discard the bags and with the experimental group and control group papers in a trash can. Dry the measuring cup and return it to your teacher.

13. Additional tests were conducted to test for the influenza virus in the remainder of the research subjects. The total results of the tests that you conducted and the additional tests are shown in the table below.
14. Complete the data table below by calculating and recording the percentage of people who have influenza viruses in their nasal mucus. *Note: There are not 100 total subjects in each group because some of the original research subjects dropped out of the research study.*

Group	Total Subjects Tested	Subjects with influenza virus in nasal mucus	Percentage of people who have influenza viruses in their nasal mucus.
Experimental (FLUSTOP)	90	18	
Control (placebo)	96	80	

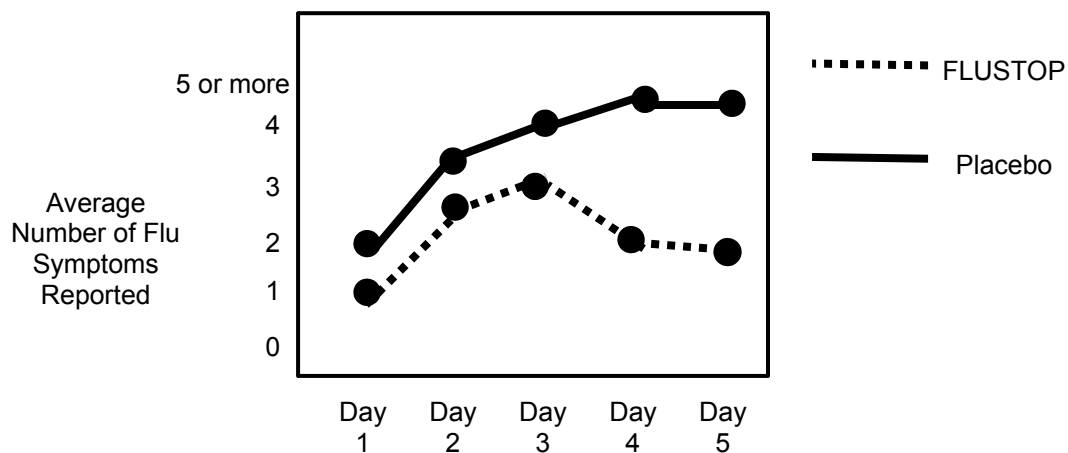
15. Use the graph grid below to make a bar graph to summarize the results of the Phase 2 Clinical Trials in the data table above. Be sure to write a scale on the vertical axis.

The Effect of FLUSTOP on the Percentage of People with Influenza Virus



16. Based on the information in your data table and bar graph, is FLUSTOP effective at preventing influenza virus infection? Explain your answer, and support your answer with information from your data table and graph.

Research subjects in the experimental group and the control group were asked to complete a survey about the flu **symptoms** that they experienced during each of the five days. The graph below summarizes the results of analyzing the surveys from the experimental group and control group.



17. Based on the information in the graph above, is FLUSTOP effective at reducing flu symptoms? Explain your answer, and support your answer with information from the graph.

18. The researchers also collected information on **side effects** that the research subjects experienced during the experiment. The table below provides information on the percent of research subjects that reported side effects.

Percent of research subjects that reported side effects	With FLUSTOP	With Placebo
Nausea (without vomiting)	6%	2%
Vomiting	3%	1%
Diarrhea	10%	7%
Bronchitis	2%	2%
Abdominal pain	2%	2%
Dizziness	3%	2%
Headache	2%	2%
Insomnia (difficulty sleeping)	1%	1%
Fatigue	1%	1%

19. Based on the information in the table above, what side effects are likely caused by FLUSTOP? Explain how you arrived at your answer.

20. Do you think these side effects are severe and frequent enough to stop further testing of FLUSTOP with larger numbers of people? Explain why or why not.

Part D: Phase 3 Clinical Trials

Phase 3 clinical trials involve a large number of research subjects so that scientists can see how FLUSTOP works in a wide variety of people. The Phase 3 clinical trial involved 3,000 research subjects. Data was collected by 50 doctors from different locations across the United States. Each doctor recruited 60 research subjects who:

- Had not been vaccinated with the influenza vaccine.
- Had recently been exposed to a family member who had the flu.

Children under the age of 12 and women who were pregnant or breast feeding were excluded (not accepted) as research subjects.

One half of the research subjects were randomly selected to be given a 5 day treatment of one FLUSTOP capsule per day. The other half of the research subjects were randomly selected to be given one placebo capsule per day for 5 days. Data was collected on day 6. The data table below summarizes the results of the Phase 3 clinical trial.

Data collected on day 6	With FLUSTOP	With Placebo
Influenza virus in nasal mucus	21%	85%
0 symptoms of flu	75%	10%
1-2 symptoms of flu	20%	30%
3 or more symptoms of flu	5%	60%
Nausea/vomiting	7%	3%
Dizziness	4%	2%
Diarrhea	10%	6%
Worsening of heart disease	4%	1%
Worsening of liver disease	7%	1%
Worsening of diabetes	6%	2%

1. Why is it important to include a large number of research subjects in a Phase 3 clinical trial?

In an experiment, the **independent variable** is the variable that is varied or manipulated by the researcher, and the **dependent variable** is the response that is measured. An independent variable is the presumed cause, whereas the dependent variable is the presumed effect.

A **controlled variable** is a variable that is held constant or kept the same in both the experimental and control group to prevent its effect on the outcome of the experiment.

Base your answers to questions 2 through 4 on the information in the box above.

2. What is the independent variable in this Phase 3 clinical trial?

3. List two dependent variables that were measured or observed in this Phase 3 clinical trial.

- _____
- _____

4. List at least two constants or controlled variables that should be kept the same in both the experimental group and the control group in this clinical trial.

- _____
- _____

5. Based on the side effects observed during the Phase 3 clinical trials, list at least two warnings that should be included in the prescription information provided for doctors or their patients.

- _____
- _____