

Developing a New Flu Prevention Drug

Core Concepts:

- Development and scientific testing of new drugs is a time consuming and expensive process.
- Clinical trials are scientific experiments used to determine if a drug is both safe and effective.

Class Time required:

3-5 forty-minute class periods

Teacher Provides:

For each student

- Copy of student handout entitled **Developing A New Flu Prevention Drug**

For each team of 2-3 students

- **Part B: Phase 2 Clinical Trials** - laboratory supplies as described below:
 - Three tubes or cups labeled “Human Volunteer 1”, “Human Volunteer 2”, and “Human Volunteer 3”. *Note: 15 ml test tubes with lids or 1 ounce portion cups with lids work well for this.* Fill the tubes or cups as shown on the chart below.

Label on tube or cup	Fill tube or cup with
Human Volunteer 1	10 ml tap water 1 drop white vinegar 2 drops 2% phenolphthalein **
Human Volunteer 2	10 ml tap water 3 drops white vinegar 2 drops 2% phenolphthalein **
Human Volunteer 3	10 ml tap water 2 drops white vinegar 2 drops 2% phenolphthalein **

**2% phenolphthalein can be purchased from most science supply companies.

- 8 plastic toothpicks or food picks or solid stirring rods
- Small tube labeled “FLUSTOP (10 mg per drop)” containing at least 2 mL of 1% washing soda solution. *Do NOT use baking soda.* Washing soda can be purchased in the laundry section of a supermarket. To make a 1% washing soda solution, mix 100 ml of water with 1 gram (scant 1/4 teaspoon) of washing soda.
- Plastic dropper labeled “FLUSTOP (10 mg per drop)”

- **Part C: Phase 3 Clinical Trials** - laboratory supplies as described below:
 - 25 mL graduated cylinder or graduated pharmacy dosing cup.
 - 2 sandwich size plastic bags labeled “For Influenza Tests” each containing 1/8 teaspoon of **washing soda** (sodium carbonate) available in laundry section of supermarket. Do NOT use baking soda (sodium bicarbonate). Be careful to place the labels on the bags so that they will not interfere with viewing the test sheets in the bags.
 - **Experimental Group Test Sheet** printed on white cardstock paper and cut to size (each group will get ¼ sheet). See page x. Spot 1 of the five circles with phenolphthalein. Use a cotton swab dipped in 1% or 2% phenolphthalein solution to make a spot in the middle circle.
 - **Control Group Test Sheet** printed on white cardstock paper and cut to size (each group will get ¼ sheet). See page xi. Spot 4 of the five circles with phenolphthalein. Use a cotton swab dipped in 1% or 2% phenolphthalein solution to make spots in the four circles on the right.
 - Access to water. Providing a cup or bottle with at least 50 mL of tap water for each group avoids need for students crowding around a sink.

Teacher Resources:

VIDEOS - The following sites provide videos that can be used as an introduction to the drug development and testing processes. Consider showing one of these videos before starting Part B and another of these videos before starting Part G.

- **How a Drug Becomes a Drug** is a 4 minute video from the National Institute of Allergy and Infectious Disease that begins with describing basic research and also describes clinical trials. <https://www.youtube.com/watch?v=U96He401wj4>
- **Introduction to How Drugs are developed** is an animated 2 minute video that describes the phases of clinical research. It is particularly engaging for below average learners as an introduction. <https://www.youtube.com/watch?v=wwDvAEmq-cM&app=desktop>
- **Medical Research** provides short videos about clinical trials. The link below opens to a video on the phases of clinical trials. Scroll down to see other brief videos about clinical trials. <http://research.emedtv.com/clinical-trials-video/different-phases-of-research-studies-video.html>
- **Clinical Drug Trial Phases Explained** is a 4 minute video describing clinical trial phases and what happens after clinical trials. <https://www.youtube.com/watch?v=1FDB8vsOE0g&app=desktop>
- **The Drug Discovery Process** a 3 minute video describing the drug discovery and clinical testing process. <https://www.youtube.com/watch?v=DhxD6sVQEYc&app=desktop>

Additional Resources:

- **The Drug Development Process** website from the FDA provides detailed information for patients about the drug development process. <http://www.fda.gov/forpatients/approvals/drugs/default.htm>
- **The FDA’s Drug Review Process: Ensuring Drugs are Safe and Effective** provides a variety of resources designed to educate the public about the drug development and approval process. <http://www.fda.gov/drugs/resourcesforyou/consumers/ucm143534.htm>
- **FDA Drug Approval Process** infographic is a great visual way to learn about the drug development process. Needs to be printed on legal size paper. <http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/UCM284393.pdf>

Note: Consider doing a Google search using the search term “drug development infographic” and printing several different types of infographics. You can ask students to evaluate which infographic was most effective in helping them complete Part B and in helping them understand and remember the drug development process.
- **Clinical Trials.gov** is a registry and results database of publically and privately supported clinical trials conducted around the world. It has a searchable database that is well worth exploring. It also provides information for patients and families. <http://www.clinicaltrials.gov>
- **NIH Clinical Research Trials and You** provides a wealth of information about clinical research, written for the general public. <http://www.nih.gov/health/clinicaltrials/index.htm>
- **Ethics in Clinical Research** web page from the NIH describes the ethical guidelines for clinical research. <http://clinicalcenter.nih.gov/recruit/ethics.html>
- **NIH Curriculum Supplement Series: Exploring Bioethics** includes information on teaching bioethics to high school students. Module 5 Research Ethics: The Power and Peril of Human Experimentation may be used as an extension to the “Developing A New Flu Prevention Drug” activity. <https://science.education.nih.gov/HighSchool/ExploringBioethics>
- **VCT Virtual Clinical Trials: Advances in Neuroscience** provides three cases in which students are involved in designing clinical trials. Requires Flash Player. Also explore the For Educators, Fun Stuff, etc. at the top of the page. <http://vct.rice.edu/>
- **The Clinical Trials Process: From Trial to Treatment** provides a concise infographic chart that compares the different phases of clinical trials. <http://visual.ly/understanding-phases-clinical-trials>

Suggested Class Procedure:

NOTE: Both animal testing and human testing involve ethical issues that may concern students. Be prepared to value their concerns. Emphasize that the FDA requires both animal and human testing before a drug can be sold as a prescription or over-the-counter medicine. The focus of this activity should remain on understanding how animal and human testing is important for ensuring that medicines are safe and effective.

Homework Prior to Day 1

1. Distribute **Developing A New Flu Prevention Drug** instructions to each student.
2. Students work individually to complete **Part A: FLUSTOP in the News**. This may be done in class or for homework.
3. Students may be concerned about animal testing using monkeys. Consider addressing the importance of testing a new drug on animals before testing it on humans.

Day 1

4. Explain that new drugs (medicines) need to be tested in humans to be sure that they are safe and effective. Scientific tests involving humans are called clinical trials.
5. Show one of the brief videos listed in the Teacher Resources as an introduction to clinical trials and the drug development process.
6. Assign students to work in teams of 2-3 students. Explain that they will be conducting experiments or interpreting data from human testing (clinical trials) for the FLUSTOP medicine.
7. Distribute materials for **Part B: Phase 1 Clinical Trials** to each team of students:
 - 10 mL measuring cup (pharmacy dosing cup) or graduated cylinder
 - 3 small tubes or cups labeled “Human Volunteer 1”, “Human Volunteer 2”, and “Human Volunteer 3”
 - 8 plastic toothpicks, food picks, or stirring rods
 - Small tube labeled “FLUSTOP (10 mg per drop)”
 - Plastic dropper labeled “FLUSTOP”
8. Students use distributed materials and work with their partner to complete **Part B: Phase 1 Clinical Trials**. *Note: Consider asking students for possible explanations for why there is variation in the amount of FLUSTOP that is safe for the three volunteers.*
9. Optional: Ask students to share their answers to questions 9-13 with another team or with the entire class.
10. Ask students to explain the purpose of Phase 1 clinical trials.
11. Be certain that students dispose of the three tubes/cups (“Human Volunteer 1-3”).

Day 2

12. Distribute materials for **Part C: Phase 2 Clinical Trials** to each team of students:
 - 25 mL graduated cylinder or graduated pharmacy dosing cup
 - 2 plastic bags labeled “For Influenza Tests” containing washing soda
 - **Experimental Group Test Sheet** spotted with phenolphthalein
 - **Control Group Test Sheet** spotted with phenolphthalein
 - Cup or bottle of water
13. Students use distributed materials and work with their partner to complete **Part C: Phase 2 Clinical Trials**.
14. Optional: Ask students to share their answers to questions 16 through 20 with another team or with the entire class.
15. Ask students explain the purpose of Phase 2 clinical trials.

Day 3

16. Students complete **Part D: Phase 3 Clinical Trials**. No additional materials are required. This is a “minds-on” rather than “hands-on” activity.
17. Optional: Use the multiple choice questions on pages vi through ix as homework or a quiz.

Multiple Choice Questions - *A New Flu Prevention Drug*

1. It is important to include a control group in a well-designed experiment so that
 - A. The experiment only includes adult males.
 - B. The control group can control what is done to other people involved in the experiment.
 - C. The results from the control group can be compared to the experimental group results.
2. A fake medication that looks like the real medication but does not contain any substance likely to have an effect is called a
 - A. Placebo.
 - B. Illegal drug
 - C. Experimental medication.
3. An experiment conducted on a small number of healthy human subjects to determine the dose of a medicine that would be safe to use for further testing on humans is called a
 - A. Phase 1 Clinical Trial.
 - B. Phase 2 Clinical Trial.
 - C. Phase 3 Clinical Trial.
4. An informed consent form for a clinical trial must include
 - A. the names of all people participating in the clinical trial
 - B. An explanation of the risks and benefits of participation in the clinical trial.
 - C. Information on whether they will be in the experimental group or the control group.
5. The main purpose for involving thousands of subjects in a Phase 3 Clinical Trial is to
 - A. Advertise the benefits of a medicine to a large number of people.
 - B. Identify people who could be featured in product advertisements for a medicine.
 - C. Determine whether a medicine is safe and effective for many different types of people.
6. Phase 4 Clinical Trials continue to study a drug's safety and effectiveness
 - A. After a drug is sold as a prescription medicine.
 - B. After a drug is sold as an over-the-counter medicine.
 - C. Until the drug is approved by the FDA for sale as a prescription medicine.
7. Researchers randomly assign research subjects to the experimental group or control group so that they can be more confident that
 - A. There are no errors in their experimental procedure and data collection.
 - B. The observed effects are due to a treatment and not to other characteristics of the groups.
 - C. Human subjects are not exposed to any risks from the experimental procedure.

Base your answers to questions 8 through 10 on the reading below.

New Drug in the Fight Against Hair Loss

Scientists announced the discovery of HAIRKEEP, a drug that prevents male pattern baldness. Male pattern baldness (MPB) occurs when hair follicles are damaged by the hormone dihydrotestosterone (DHT). HAIRKEEP is a small molecule that binds to hair follicle cells and blocks the action of DHT.

Tests using rats treated with HAIRKEEP have shown that it was effective in maintaining the health of hair follicle cells. Recently, University of Fiction scientists administered HAIRKEEP injections to an experimental group of 20 monkeys for 10 days. For a comparison, a control group of 20 other monkeys was given a placebo (injection of water) for 10 days. Microscopic examination of hair follicles in both groups of monkeys revealed that 80 % of the monkeys who received a placebo had damaged hair follicles. Only 10% of the monkeys who were treated with HAIRKEEP had damaged hair follicles.

In the future, HAIRKEEP may be used by humans to prevent hair loss in people who have inherited the male pattern baldness gene. Scientists caution, however, that human testing is needed to provide evidence that HAIRKEEP is both safe and effective for use by humans.

8. The monkeys who received a placebo were
 - A. The control group.
 - B. Given lower doses of HAIRKEEP.
 - C. Selected because they had healthy hair follicles.

9. Scientists tested HAIRKEEP on animals because
 - A. HAIRKEEP is only effective when used in rats and monkeys.
 - B. Animals are less likely than humans to be harmed by HAIRKEEP.
 - C. Animal tests may reveal that HAIRKEEP is not safe and should not be tested on humans.

10. According to the article, which step in the drug development and testing process has not been completed?
 - A. Research to determine the cause of male pattern baldness.
 - B. Research to identify a substance that may prevent male pattern baldness.
 - C. Research to provide evidence that HAIRKEEP may prevent human male pattern baldness.

11. The data table below shows the results of testing HAIRKEEP on 3 healthy human subjects to determine the dose of HAIRKEEP that would be safe for humans.

Human Subjects #	Highest dose of HAIRKEEP that did <u>not</u> result in harmful effects (milligrams per injection)
1	20
2	30
3	10

What is the highest dose of HAIRKEEP that should safely be used for human testing on larger numbers of subjects?

- A. 10 milligrams per injection
- B. 20 milligrams per injection
- C. 30 milligrams per injection

Base your answers to questions 12 through 15 on the information below.

Researchers conducted a Phase 2 clinical trial to determine if HAIRKEEP was safe and effective for preventing male pattern baldness. They enrolled 100 male subjects who had inherited at least one gene for male pattern baldness. At the beginning of the experiment, researchers counted the number of hairs in 1 square centimeter of scalp for each of the subjects. Subjects were given a weekly injection of either HAIRKEEP or a placebo for one year. At the end of the year, researchers counted the number of hairs in 1 square centimeter of scalp and calculated the percentage hair loss for each subject.

12. For an experiment to determine if HAIRKEEP is effective, which treatment should be given for one year to the control group subjects?
- A. Treatment with HAIRKEEP
 - B. Treatment with a placebo
 - C. Treatment with DHT (a hormone that causes male pattern baldness)
13. Random assignment to create an experimental group and a control group for an experiment would best be accomplished by assigning
- A. Bald people to the experimental group and people with hair to the control group.
 - B. Males to the experimental group and females to the control group.
 - C. Subjects to an experimental treatment or control treatment by chance (like the flip of a coin).

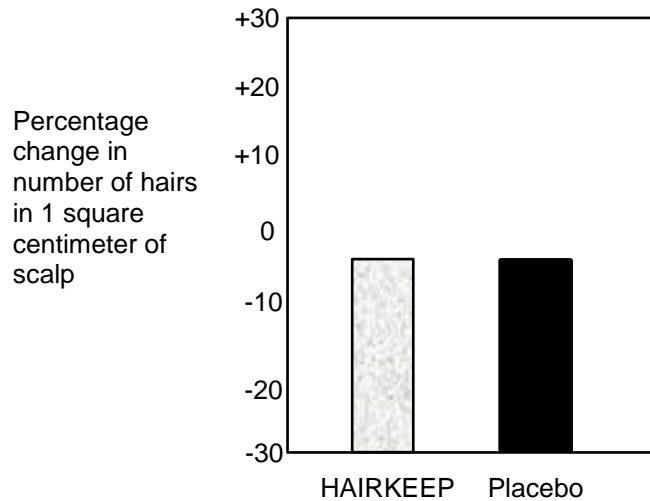
14. The researchers also collected information on side effects that the subjects experienced during the experiment.

Percent of research subjects that reported side effects	With HAIKKEEP	With Placebo
Dizziness	2%	3%
Headache	10%	2%
Insomnia	10%	10%
Fatigue	5%	1%

Based on the information in the table above, what side effects are likely caused by HAIKKEEP?

- A. Headache and fatigue
- B. Headache and dizziness
- C. Headache and insomnia






15. The graph below shows the results of the Phase 2 clinical trial.








According to the information in the graph, HAIKKEEP

- A. Is effective for preventing hair loss.
- B. Is effective for treating hair loss.
- C. Is not effective for reducing hair loss.






Experimental Group Influenza Test Sheet

				
Subject 1	Subject 2	Subject 3	Subject 4	Subject 5






Experimental Group Influenza Test Sheet

				
Subject 1	Subject 2	Subject 3	Subject 4	Subject 5






Experimental Group Influenza Test Sheet

				
Subject 1	Subject 2	Subject 3	Subject 4	Subject 5






Experimental Group Influenza Test Sheet

				
Subject 1	Subject 2	Subject 3	Subject 4	Subject 5






Control Group Influenza Test Sheet

				
Subject 1	Subject 2	Subject 3	Subject 4	Subject 5






Control Group Influenza Test Sheet

				
Subject 1	Subject 2	Subject 3	Subject 4	Subject 5

Control Group Influenza Test Sheet

				
Subject 1	Subject 2	Subject 3	Subject 4	Subject 5

Control Group Influenza Test Sheet

				
Subject 1	Subject 2	Subject 3	Subject 4	Subject 5

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.

The experimental group was a group of 20 monkeys who received a FLUSTOP pill for 5 days

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

The control group was a group of 20 monkeys who received a placebo pill (a pill that does not contain FLUSTOP) for 5 days

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

A control group provides a basis of comparison. OR You can compare the results of the experimental group to the results of the control group to determine if the drug works.

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?

The placebo is a pill that does not contain FLUSTOP.

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

The purpose of the placebo is to show what happens if the animals get a substance that you know does not have an effect.

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

Scientists test FLUSTOP on animals to determine if FLUSTOP works to prevent influenza and if it is safe when used in animals. If it is not safe for animals, then it is probably not safe for 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?

To be sure the research subjects understood the risks involved in Phase 1 clinical trials.

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			

Student answers will vary depending on dropper size. Volunteer 1 should require the smallest number of drops and Volunteer 2 should require the largest number of drops.

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? _____
Student answers will vary. Look at the data table to find the volunteer with the lowest number of drops
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.
If people were given the average dose, some people who were more sensitive to FLUSTOP may be harmed.
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). ***50 – 80 mg***
NOTE: It is important to look at the data the students recorded in the data table above. The results may vary from 5-8 drops or 50-80 mg.
10. Explain why it was important to test the FLUSTOP on more than one volunteer.
Because the results vary for different volunteers and it is important to find out the dose that is safe for people who may be more sensitive to the harmful effects of FLUSTOP. or Everyone has a different tolerance for the drug. You get a better idea of the appropriate dosage by comparing several people's results.
11. **Summarize:** Explain the purpose for Phase 1 Clinical Trials.
Phase 1 Clinical Trials are used to determine a safe dose to be used for future human testing.
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?

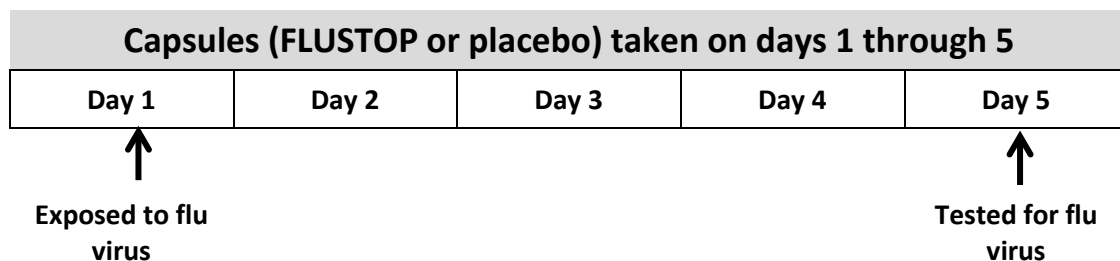
A Phase 2 clinical trial is a scientific experiment used to determine if a drug is safe and effective for use by humans.

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

Random assignment is used to create experimental and control groups that are approximately the same at the beginning of the experiment. For example, researchers do not want to put all of the sickest people in one group because that would affect the results.

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.

They should know that they will be exposed to the flu virus, that they will be confined to a hospital for 5 days, and that they may develop mild to serious flu symptoms.

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

*The experimental group is given a FLUSTOP capsule.
The control group is given a placebo capsule.*

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

They were both exposed to the flu virus on day 0 or they were both tested for flu virus on day 5.

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)	4	1	5	20%
Control (placebo)	1	4	5	80%

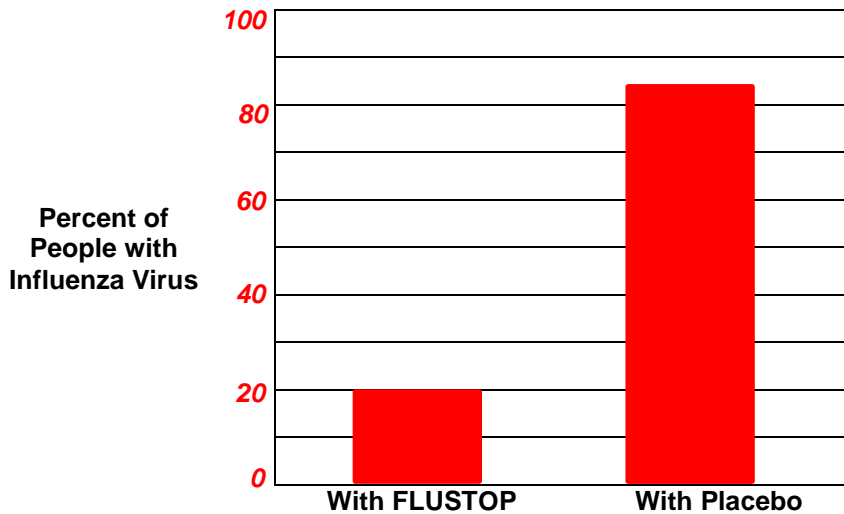
12. **Cleanup:** Discard the bags and with the experimental group and control group papers in a trash can. Dry the measuring cup and return it to your teacher.

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	20%
Control (placebo)	96	80	83.3%

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.

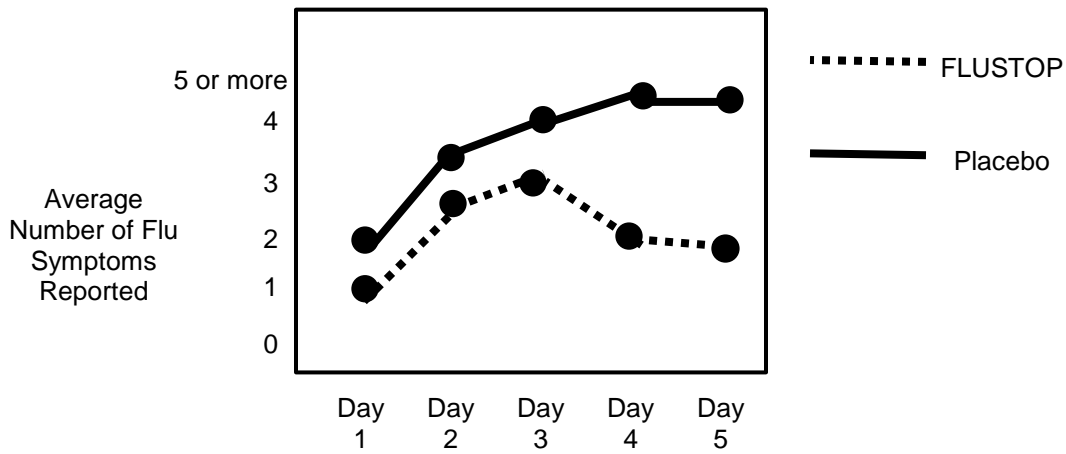
The Effect of FLUSTOP on the Percentage of People with Influenza Virus



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.

FLUSTOP is effective at preventing influenza. 83.3 % of the people who did not use FLUSTOP had viruses in their mucus. Only 20% of the people who used FLUSTOP had viruses in their mucus. Students may note that FLUSTOP did not completely prevent the flu, it only reduced the chances of getting the flu.

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.

FLUSTOP is effective in preventing flu symptoms. People who took FLUSTOP had fewer flu symptoms than people who took the placebo.

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.

Nausea (without vomiting), vomiting, diarrhea, and dizziness because these were greater in the people who got FLUSTOP than in the group that got the placebo.

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.

Student answers will vary but most will conclude that these symptoms are minor compared to the symptoms of the flu OR that it is better to have minor discomfort if the result is fewer people will get influenza.

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?

It is important to include large numbers of subjects so that scientists can see how FLUSTOP works in many different types of people.

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?

Treatment with FLUSTOP or a placebo

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

- ***Percentage of subjects who had flu viruses***
- ***Number of flu symptoms***
- ***Side effects***

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.

- ***All subjects took a capsule for days 1-5.***
- ***All subjects had been exposed to a family member who had the flu.***
- ***Data was collected 6 days after the experiment began.***
- ***None of the subjects had the flu prior to clinical study.***
- ***None of the subjects had a flu vaccine.***
- ***There were equal numbers of subjects in the control group and experimental group.***

Accept other reasonable answers.

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.

- ***Patients with diabetes, liver disease, and heart disease should not take FLUSTOP or should consult their doctor before taking FLUSTOP.***
- ***Pregnant women should not take FLUSTOP.***
- ***Women who are breastfeeding should not take FLUSTOP.***
- ***Children under the age of 18 should not take FLUSTOP.***