UNIVERSITY of MARYLAND
BALTIMORE

RESEARCH CONSENT FORM AND HIPAA AUTHORIZATION

v2.0; 07 OCT 2019

Project Title: A Controlled Human Infection Study of Influenza A/Bethesda/MM2/H1N1 Virus (A/California/04/2009/H1N1-like) in Healthy Subjects to Assess the Effect of Pre-Existing Immunity on Symptomatic Influenza Virus Infection

Study No.: HP-00087487

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Sponsor: National Institutes of Health (NIH) /
National Institute of Allergy and Infectious Diseases (NIAID)/Division of Microbiology and Infectious Diseases (DMID)

CONCISE SUMMARY

This is a research study to understand what happens when a person is infected with influenza ("flu") and how the body controls the infection. To do this, we will infect healthy participants ("challenge") with a strain of the flu and follow them to see what symptoms occur and when they occur. We will draw blood and take nose swabs and nose washes before we infect participants to understand if having antibodies in the blood or nasal fluid can protect from the flu infection or lead to a milder flu illness. We will also draw blood and take nose swabs and nose washes after we infect the participants to understand how and when the body's immune response to flu occurs.

If you agree to take part in this study, your involvement will last for approximately 4 months, including screening. The following visits/procedures will take place:

- A screening evaluation will take about 4 hours. This may be done in one or more visits.
- An inpatient "challenge" unit stay of at least 10 days, and perhaps longer. During the first two days of this stay, additional tests, including blood tests, urine tests, nose swabs and nose washes will be done. On the third day, blood will be drawn, and the flu virus will be given.

- If we have too many people who are eligible and are willing to participate in the study, we may need to send a few people home before the flu virus infection. You may be selected to leave the unit. If so, your study participation will end at this time. Samples that we have already collected will be kept and used for testing, as specified in the procedures section of this consent.
- Participants who remain will be given the flu virus once in their noses and will be asked to stay in the inpatient challenge unit for at least the next 7 nights and 7 days after the challenge, or until they do not have any flu virus present in their noses if longer than 7 days.
- Once you receive the flu virus in the challenge unit:
    - Samples from your nose will be taken each day to check for viruses and, on certain days, other immune responses.
    - Blood will be drawn 1 day, 3 days, 5 days and 7 days after challenge.
    - If on day 8 (7 days after the challenge) you still have flu virus found in your nose, we will offer you a medicine to treat the flu and ask you to stay in the challenge unit until you don't have any flu found in your nose for 2 consecutive days.
    - If on day 8 you still have fever or are clinically ill, we will ask you to stay in the challenge unit until your symptoms improve.
- After you leave the challenge unit, there will be 3 more clinic visits with blood draws and nose washes which will take about 45 minutes each.
- At the end of the study there will be one phone call which will take about 10 minutes.

The risks involved in joining this study are described in detail below. Some of the more common risks include symptoms of flu (mild fever, tiredness, body aches, chills, headache, blocked or runny nose, sore throat, cough and sneezing), minor pain and bruising with blood draws, and discomfort in the nose or gagging with nose sample collection. In total, we will draw approximately 85 - 105 teaspoons (approximately 424 - 525 milliliters) of your blood over the course of the research study.

Your alternative to participation is to choose not to participate.

If you are interested in learning more about this study, please continue reading below.

PURPOSE OF STUDY

This is a research study. We are inviting you to participate in this research study because you are in good health and aged 18 to 49 years.

The purpose of this research study is to understand how antibodies that you have from other flu episodes may keep you from getting flu again, what happens when a person is infected with flu

(how you feel and how your body reacts), and how the immune system responds to infection with flu (what antibodies are formed or increased after you get the flu).

The influenza virus (a germ) or "flu" virus causes influenza or "flu", an infection of your nose, throat, windpipe and your lungs. Flu is spread from person-to-person mainly through coughing and sneezing. When someone has the flu they usually have a mild fever, tiredness, body aches, chills, headache, blocked or runny nose, sore throat, cough and/or sneezing. While in most healthy people, the flu causes illness that often looks like the "common cold" and gets better on its own, it can become more serious. Children younger than 5 years of age, adults older than 65 years of age, pregnant women and people of all ages with chronic medical illnesses are more likely to get sick with the flu and have a higher risk of death from flu-related illnesses. Flu causes an average of 20,000-40,000 deaths each year in the United States (US), and most of these deaths occur in people over 65 years of age.

When the flu virus attacks your body, the immune system in your body makes proteins including antibodies that help your body fight the infection. Later, if you are exposed to the flu, your antibodies will help attack and kill the virus. With these antibodies, you may not get sick at all, or you may have a much shorter or milder illness.

By the time we are adults, we have been infected with flu many times. While we have learned a lot about how flu infects people, it is hard to know exactly when someone is exposed to flu, and what happens early on after they are exposed to flu but before they become sick. Flu "challenge" studies, where we give a strain of the flu virus to a participant, allow us to follow people closely before and after infection. We learn about the flu virus and the body's reaction to it. This may help us to design better flu vaccines or better drugs to treat flu.

Flu can be caused by different types of flu viruses. One of those flu viruses is called influenza A/H1N1. In this study, we will infect participants with a strain similar to the H1N1 virus that has been around and causing flu in people for about 10 years. This strain has been used in challenge studies to infect about 400 participants at the National Institutes of Health (NIH) and has caused mild to moderate flu symptoms.

This study will be done at 4 sites in the US, and we anticipate that up to 80 people will be challenged with the flu virus as part of this study, with approximately 20 participants at each site.

PROCEDURES

Screening Clinic Visit(s) - approximately 4 hours

At the screening visit, you will be given information about the study and asked to read this informed consent. We will ask you to read the consent and we will answer your questions. After you have had time to think about whether to participate in the study and have discussed it with your family, friends or doctor, if you wish, you will be asked to sign this consent agreeing to take part in the study.

If you agree to take part in the study, the following screening procedures will be done to see if you are eligible for this study. They may be done all in one visit, or you may be asked to return for certain parts of the screening process (for example, the chest x-ray):

- You will be asked about your complete medical history including any medications you are taking or have recently taken, vaccinations you have received, smoking history (including e-cigarettes), and alcohol and drug use over the last year.
- Your temperature, pulse, breathing rate, blood pressure and a measure of the oxygen in your lungs (O_2 saturation) will be taken.
- We will measure your height and weight.
- You will have a physical examination.
- Women who are able to become pregnant must use an acceptable method of birth control for at least 30 days before the flu virus is given until the end of the study. They will have a serum pregnancy test at this visit, and up to two more urine pregnancy tests before the flu virus is given. If the pregnancy test is positive at any time, they will not be able to continue in the study.
- We will draw approximately 15 mL (about 3 teaspoons) of blood from a vein in your arm for laboratory tests. This will include tests to see if you are infected with hepatitis B, hepatitis C, or HIV, the virus that causes AIDS.
- You will have a urine drug test for amphetamines, cocaine, and opiates now and on admission to the challenge unit.
- You will have a urine drug test for marijuana on admission to the challenge unit.
- You will have an electrocardiogram (ECG) performed.
- You will have a chest x-ray performed. Women of childbearing potential will have to have a negative serum pregnancy test before having a chest x-ray. If more than 7 days have passed since the negative serum pregnancy test, we will do a urine pregnancy test to ensure they are not pregnant before doing a chest x-ray.

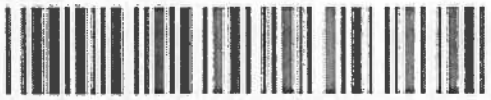
If any of the above screening tests are abnormal, you will not be able to continue in the study. Abnormal test results will be provided to you for follow-up with your provider.

After the screening visit or visits, if you are eligible to participate in the study, you will be scheduled for the inpatient challenge part of the study. We will inform you of the medications that you should not use within 7 days of your inpatient stay.

<u>Inpatient Challenge Stay (minimum 10 days)</u>
You will be admitted to the inpatient challenge unit 2 days before we plan to give the flu virus.

Inpatient Day 1 (Study Day -2)

- You will be asked if you want to continue in the study.



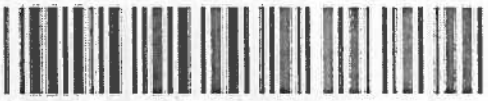
- You will be asked about your medical history including any current or new medications you are taking or have recently taken. You will be asked about recent alcohol use.
- Your temperature, pulse, breathing rate, blood pressure and a measure of the oxygen in your lungs (O_2 saturation) will be taken.
- We will measure your weight.
- You will have a physical examination.
- Women who are able to become pregnant will have a urine pregnancy test. If this is positive, they will not be able to continue in the study.
- You will have a urine drug test for amphetamines, cocaine, opiates and marijuana. If this is positive, you will not be able to continue in the study.
- You will have a swab of your nose to be sure you don't already have flu or any other respiratory virus. If this is positive, you will not be able to continue in the study.
- You will have a wash of your nose for baseline immune tests.
- We will draw about 78 1/2 mL (about 5-6 tablespoons) blood for baseline immune tests.

Inpatient Day 2 (Study Day -1)

- You will be asked if you want to continue in the study.
- You will be asked about any current or new medications you are taking or have recently taken.
- Your temperature, pulse, breathing rate, blood pressure and a measure of the oxygen in your lungs (O_2 saturation) will be taken.
- You will have a physical examination.
- You will have a swab of your nose to be sure you don't already have flu or any other respiratory viruses. If this is positive, you will not be able to continue in the study.
- You will be trained on the influenza patient-related outcomes (Flu-PRO) questionnaire and diary that you will fill out each day to record your body's reaction to flu virus.

Inpatient Day 3 (Study Day 1 – the day flu virus is given)

- You will be asked if you want to continue in the study.
- You will be asked about your medical history including any current or new medications you are taking or have recently taken.
- Your temperature, pulse, breathing rate, blood pressure and a measure of the oxygen in your lungs (O_2 saturation) will be taken.
- You will have a physical examination.
- If we have too many people who are eligible and willing to participate in the study, we may need to send some home. You may be selected to leave the unit at this time. If so, your study participation may end at this time.
- If you stay in the unit:
    - We will draw about 2 1/2 mL (less than one teaspoon) blood for baseline immune tests.



- We will give you about 2 mL of fluid containing the flu virus, about one mL (<1/4 teaspoon) in each nostril.
- We will monitor you and check the following 3 times per day while you are awake: temperature, pulse, breathing rate, blood pressure and a measure of the oxygen in your lungs (O_2 saturation)
- You will complete the Flu-PRO questionnaire and diary in the late afternoon at approximately the same time daily.
- You will be asked if there have been any changes in your health.

Inpatient Day 4 (Study Day 2)

- You will be asked about your medical history including any current or new medications you are taking or have recently taken.
- You will have your temperature, pulse, breathing rate, blood pressure and a measure of the oxygen in your lungs (O_2 saturation) taken three times a day while you are awake.
- You will have a physical examination.
- We will draw about 17 1/2 ml (about 4 teaspoons) blood for safety tests and immune tests.
- You will have a swab of your nose to see if you have flu or any other respiratory viruses.
- You will have a wash of your nose for immune tests.
- You will complete the Flu-PRO questionnaire and diary in the late afternoon at approximately the same time daily.

Inpatient Day 5 (Study Day 3)

- You will be asked about your medical history including any current or new medications you are taking or have recently taken.
- You will have your temperature, pulse, breathing rate, blood pressure and a measure of the oxygen in your lungs (O_2 saturation) taken three times a day while you are awake.
- You will have a physical examination.
- You will have a swab of your nose to see if you have flu or any other respiratory viruses.
- You will complete the Flu-PRO questionnaire and diary in the late afternoon at approximately the same time daily.

Inpatient Day 6 (Study Day 4)

- You will be asked about your medical history including any current or new medications you are taking or have recently taken.
- You will have your temperature, pulse, breathing rate, blood pressure and a measure of the oxygen in your lungs (O_2 saturation) taken three times a day while you are awake.
- You will have a physical examination.
- We will draw about 72 1/2 ml (about 5 tablespoons) blood for safety tests and immune tests.
- You will have a swab of your nose to see if you have flu or any other respiratory viruses.
- You will have a wash of your nose for immune tests.

- You will complete the Flu-PRO questionnaire and diary in the late afternoon at approximately the same time daily.

Inpatient Day 7 (Study Day 5)

- You will be asked about your medical history including any current or new medications you are taking or have recently taken.
- You will have your temperature, pulse, breathing rate, blood pressure and a measure of the oxygen in your lungs (O_2 saturation) taken three times a day while you are awake.
- You will have a physical examination.
- You will have a swab of your nose to see if you have flu or any other respiratory viruses.
- You will complete the Flu-PRO questionnaire and diary in the late afternoon at approximately the same time daily.

Inpatient Day 8 (Study Day 6)

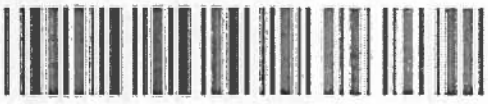
- You will be asked about your medical history including any current or new medications you are taking or have recently taken.
- You will have your temperature, pulse, breathing rate, blood pressure and a measure of the oxygen in your lungs (O_2 saturation) taken three times a day while you are awake.
- You will have a physical examination.
- We will draw about 60 ml (about 4 tablespoons) blood for immune tests.
- You will have a swab of your nose to see if you have flu or any other respiratory viruses.
- You will have a wash of your nose for immune tests.
- You will complete the Flu-PRO questionnaire and diary in the late afternoon at approximately the same time daily.
- An ECG will be performed.

Inpatient Day 9 (Study Day 7)

- You will be asked about your medical history including any current or new medications you are taking or have recently taken.
- You will have your temperature, pulse, breathing rate, blood pressure and a measure of the oxygen in your lungs (O_2 saturation) taken three times a day while you are awake.
- You will have a physical examination.
- You will have a swab of your nose to see if you have flu or any other respiratory viruses.
- You will complete the Flu-PRO questionnaire and diary in the late afternoon at approximately the same time daily.

Inpatient Day10 (Study Day 8)

- You will be asked about your medical history including any current or new medications you are taking or have recently taken.
- You will have your temperature, pulse, breathing rate, blood pressure and a measure of the oxygen in your lungs (O_2 saturation) taken three times a day while you are awake.
- You will have a physical examination.



- We will draw about 87 1/2 ml (about 6 tablespoons) blood for safety and immune tests.
- You will have a swab of your nose to see if you have flu or any other respiratory viruses.
- You will have a wash of your nose for immune tests.
- You will complete the Flu-PRO questionnaire and diary. You may complete the Flu-PRO earlier in the day than previous days if you are being discharged to home.
- If you meet discharge criteria (two consecutive days with nose swabs negative for flu virus; no fever, and are clinically stable for two days), you will be discharged from the inpatient unit.
- If there is still virus found in your nasal swab, you will be offered one dose of baloxavir, an antiviral drug and you will not be discharged.
- If you do not have virus found in your nasal swab, but still have fever or are clinically ill, an appropriate work-up will be done and you will not be discharged.

Inpatient Day 11-Day 14 (Study Days 9-12 if you are not discharged on Day 8).

- You will be asked about your medical history including any current or new medications you are taking or have recently taken.
- Your temperature, pulse, breathing rate, blood pressure and a measure of the oxygen in your lungs (O_2 saturation) will be taken three times a day while you are awake.
- You will have a physical examination.
- You will have a swab of your nose to see if you have flu or any other respiratory viruses.
- You will complete the Flu-PRO questionnaire and diary in the late afternoon at approximately the same time daily.
- If you meet discharge criteria (two consecutive days with nose swabs negative for flu virus; clinically stable for two days and no fever on the day of discharge), you will be discharged from the inpatient unit.
- If there is still virus found in your nasal swab, you will be offered one dose of baloxavir if you did not receive one before, and you will not be discharged.
- If you remain clinically ill or have a temperature, appropriate clinical work-up will be done and you will not be discharged.

Post-discharge through Study Day 14

- You will complete the Flu-PRO questionnaire and diary in the late afternoon at approximately the same time daily.

Post-discharge Clinic Visit 1 (Study Day 15) – approximately 45 minutes

- You will be asked about your medical history including any current or new medications you are taking or have recently taken.
- You will have your temperature, pulse, breathing rate and blood pressure taken.
- You will have a physical examination.
- We will draw about 56 ml (about 4 tablespoons) blood for immune tests.
- You will have a wash of your nose for immune tests.
- We will collect the Flu-PRO questionnaire and diary.

Post-discharge Clinic Visit 2 (Study Day 29)– approximately 45 minutes

- You will be asked about your medical history including any current or new medications you are taking or have recently taken.
- You will have your temperature, pulse, breathing rate and blood pressure taken.
- You will have a physical examination.
- We will draw about 68 ml (about 4 1/2 tablespoons) blood for immune tests.
- You will have a wash of your nose for immune tests.

Post-discharge Clinic Visit 3 (Study Day 61)– approximately 45 minutes

- You will be asked if there have been any changes in your health and about any new medications you are taking or have recently taken.
- You will have your temperature, pulse, breathing rate and blood pressure taken.
- You will have a physical examination.
- We will draw about 68 ml (about 4 1/2 tablespoons) blood for immune tests.
- You will have a wash of your nose for immune tests.

Telephone follow-up (Study Day 91)– approximately 10 minutes

- You will be asked if there have been any serious changes in your health.

Early Termination Visit – approximately 45 minutes

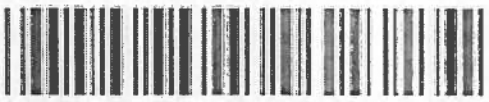
If you decide to leave the study early, we will ask you to complete a final study visit. At this visit, the following may be done:

- You will be asked about your current health and any changes in your medications.
- We may ask you about the Flu-PRO questionnaire and diary.
- You may have a physical examination based on your current health.
- You may have your vital signs taken - temperature, pulse, breathing rate and blood pressure.
- We may collect blood or nasal washes for study or safety tests.
- Other assessments may be done depending on when this visit occurs during the study period.

Unscheduled Study Visits – approximately 30 minutes

Unscheduled visits may occur for further evaluations. At these visits, the following may be done:

- You will be asked about your medical history including any current or new medications you are taking or have recently taken
- We may ask you about the Flu-PRO questionnaire and diary.
- You may have a physical examination based on your health.
- You may have your vital signs taken - temperature, pulse, breathing rate and blood pressure.



- We may collect blood or nasal washes for safety or study tests.
- Other assessments may be done depending on when this visit occurs during the study period.

BLOOD AND NASAL SAMPLE STORAGE FOR FUTURE USE

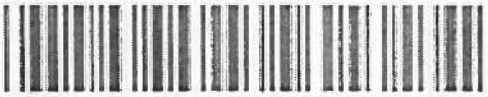
As part of this study, we are obtaining blood and nasal samples from you. However, we may not need all of the blood or nasal samples that we collect for this research study. We would like to store the extra blood and nasal samples and use these excess/leftover blood and nasal samples and your information collected during this study for future research. Types of research include new or different immunological laboratory tests to provide information for the development of new flu vaccines, or to better understand flu or other infections. If you agree below, new genetic testing including whole genome sequencing (DNA testing) may occur. The tests we might want to use to study your blood and nasal samples may not even exist at this time.

The excess/leftover blood and nasal samples for future research will be stored indefinitely at a site determined by the study sponsor, NIH. Each blood and nasal sample will be labeled only with a barcode and a unique tracking number to protect your confidentiality. Personnel at the storage facility and testing lab will not know your identity, or the volunteer ID code assigned to you for the study. However, the researchers who enrolled you will keep a code key in a secure area that could connect barcodes or tracking numbers to identify you, if needed.

Stored excess/leftover blood and nasal samples will be used only for research purposes. At any time during this study or after this study is over, stored excess/leftover blood and nasal samples may be shared with other investigators, institutions or drug companies. The samples will not be sold or used directly for production of any commercial product. There are no benefits to you in the collection, storage and future use of your blood and nasal samples. The results of any future testing will be kept confidential in the same way as the results of other testing done for this study.

You may change your mind and withdraw consent for future use of your excess/leftover samples at any time. You will need to contact Dr. Neuzil or a research team member at 410-706-6156. Your blood and nasal samples will be removed from the study repository when the study is completed.

Please feel free to ask the study staff any questions you may have about how your blood samples may be used.



If you choose to participate, please initial your understanding about permission for us to use your excess/leftover blood and nasal samples for future research.

_____ YES, I give permission that my excess/leftover blood and nasal samples may be stored for an indefinite period of time and used for future research. I may withdraw my consent at any time.

_____ NO, I do not give permission that my excess/leftover blood and nasal samples may be stored for an indefinite period of time and used for future research.

GENETIC TESTING

We will perform genetic testing on your blood sample if you give your consent. The genetic testing that is performed as part of this study is called HLA typing, and transcriptomics. This genetic testing will look at how particular genes and variations in those genes might relate to how your body responds to the flu virus.

If you consent, future genetic testing with your left-over samples may include DNA testing.

Following genetic testing, and with your consent, your genetic testing information may be shared with other researchers. We may share your genetic information (data) through a "closed" database, also called a restricted data repository. NIH gives permission to other researchers to use your genetic information for research. To qualify, researchers must receive approval from NIH to access and use the research information. Types of future research using your data may be related to the research in this study or other types of research. Your individual data will not contain information that can easily identify you. It may be possible to identify you with your DNA; however, the researchers must follow rules specifically to not identify you. If you change your mind and want to remove your data from the database, you should contact Dr. Neuzil or a research team member at 410-706-6156. If possible, your information will be removed for future research. Your data cannot be removed from research studies it has already been used for.

Please initial your decision for us to use your information and blood samples for genetic research for this research study:

_____ YES, you may use my information and samples for genetic research for this study and future research.

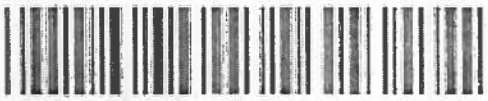
_____YES, you may use my information and samples for genetic research as required for this study. Information may be shared for future research, but no new genetic testing with my samples may occur.

_____ NO, you may not use my information and samples for genetic research.

WHAT ARE MY RESPONSIBILITIES IF I TAKE PART IN THIS RESEARCH?

If you take part in this research, you will be responsible to do the following:

- come to all study visits as scheduled



- agree to remain in the inpatient challenge unit after the flu virus is given until all discharge criteria are met
- complete the Flu-PRO questionnaire and diary during the inpatient stay and for up to 7 days afterwards
- avoid receiving a licensed or investigational vaccine within 30 days before the flu virus challenge.
- avoid receiving the 2019/2020 seasonal influenza vaccine within 60 days after receipt of the flu virus challenge.
- If you are a woman of childbearing potential, avoid pregnancy by practicing true abstinence or at least 2 acceptable forms of birth control from at least 30 days before the flu virus challenge until one week after discharge from the inpatient unit, and at least 1 acceptable form of birth control from one week after discharge until the end of the study.
- abstain from alcohol use 7 days before inpatient stay, and throughout the inpatient stay
- avoid using prohibited medications 7 days before and during your inpatient stay.
- avoid eating or drinking anything hot or cold within 10 minutes prior to oral temperature being taken
- abstain from donating blood for 2 months before and for the duration of the study

POTENTIAL RISKS AND DISCOMFORT

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be risks in this study which are not yet known.
The potential risks of participating in this trial are those related with having blood drawn, receiving a flu virus in your nose, and having other procedures performed.

Risks of receiving flu virus in the nose

You are likely to experience symptoms from the flu virus given in your nose. Typical symptoms include mild fever, tiredness, body aches, chills, headache, blocked or runny nose, sore throat, cough and sneezing. These symptoms usually last for 3-4 days. Symptoms may last for up to two weeks, but this is unusual.

A similar virus to the one used in this study has been given to more than 400 participants as part of challenge studies. No significant safety issues have been identified, and no severe or complicated cases of influenza have occurred. The challenge has been made specifically for human infection under the strictest conditions. It has been carefully tested to ensure it is free from other bacteria or viruses.

Guillain-Barré syndrome (GBS) is a rare disease of the nerves that causes weakness, below normal or no reflexes, and a high amount of protein in the cerebrospinal fluid (fluid found in the brain and spinal cord). Influenza virus infection has been associated with GBS. Most people get better completely, but some people can be paralyzed for a long time. Anyone can develop GBS, but people older than 50 are at greatest risk.

While rare in healthy persons, natural flu virus may cause more severe illness, including high fever, sinus infection, bronchitis, pneumonia, respiratory distress, heart problems including an inflammation of the heart muscles (myocarditis), neurological complications and even death. You will be followed closely with attention to these possible risks.

Risks related to blood draws

Having blood taken from your arm can cause temporary pain and discomfort, bruising and fainting with a rare risk of infection. A possible risk of giving blood may be a low blood count (anemia), however, the total amount for this study is lower than donating a unit of blood so the risk of anemia is low.

Risk related to nose swabs or nose washes

Obtaining nose fluid or a nose swab can cause discomfort in the nares, a gag reflex, bleeding from the nose, watery eyes, or coughing at the time of collection.

Risks of chest x-ray

We are exposed to naturally occurring background radiation every day. The radiation dose people get from a single chest x-ray is similar to the risk that occurs naturally over the course of 10 days. There is a greater risk to a developing fetus. Female participants will have a urine pregnancy test before the chest x-ray. Pregnant and breastfeeding women may not participate in this study.

Risks of electrocardiogram (ECG)

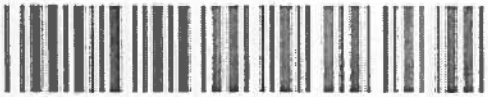
The electrodes of an ECG may feel cold when applied; in rare cases, a rash or skin irritation develops where the patches are placed. This type of irritation usually resolves by itself, but topical medication is occasionally required.

Risks of baloxavir marboxil antiviral

Adverse events reported in at least 1% of adult and adolescent subjects treated with baloxavir marboxil included diarrhea (3%), bronchitis (2%), nasopharyngitis (1%), headache (1%) and nausea (1%). The flu virus we are using is sensitive to this medicine.

Risks of delaying influenza vaccine receipt

In the US, routine annual influenza vaccination is recommended for all persons, with an emphasis placed on vaccination of high-risk groups and their caregivers. To participate in this study, you are asked to delay the 2019-2020 influenza season vaccination through 60 days after the flu virus challenge. The flu vaccine takes approximately two weeks to be protective. If the influenza season begins before this time, you will be at increased risk of developing influenza illness. Influenza illness is described above.



Risks of Genetic Testing

Since your genetic data, and health information may be stored and shared with other researchers, there may be a risk that information resulting from research genetic testing could be misused for discriminatory purposes. However, state and federal laws provide some protections against genetic discrimination. If you have any questions, please ask your Principal Investigator. Researchers who will have access to genetic information about you will take measures to maintain the confidentiality of your information as described below. Risks may also result if you disclose information yourself or give separate consent to have your research records released.

For women participating in the study

A pregnancy test will be performed on all women of childbearing potential at the first screening appointment, before the chest x-ray, and when admitted to the inpatient unit. Pregnant and breast-feeding women may not participate in this study, as pregnant women, the developing fetus and newborns are at increased risk of complications from influenza virus infection. You must confirm to the best of your knowledge that you are not pregnant and do not intend to become pregnant. Women of childbearing potential in a heterosexual relationship must agree to use or have practiced true abstinence or use two acceptable forms of contraception for 30 days prior to the flu virus challenge, until one week after discharge from the inpatient unit and use at least one acceptable form of contraception through the end of the study.

POTENTIAL BENEFITS

You will receive no direct benefit from taking part in this study. There may be benefits to society through the improvement of our understanding of flu infection, how humans are protected from flu and the immune responses that occur after flu infection.

ALTERNATIVES TO PARTICIPATION

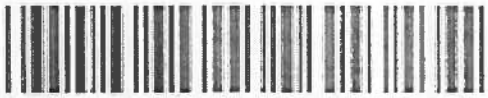
This is not a treatment study. Your alternative is to not take part. If you choose not to take part, your healthcare at University of Maryland, Baltimore will not be affected.

COSTS TO PARTICIPANTS

It will not cost you anything to take part in this study.

COMPENSATION TO PARTICIPANTS

You will be offered compensation for your time and inconvenience for each of the events of the study: screening visit(s), inpatient stay, Flu-PRO and diary completion, follow-up clinic visits, telephone call(s) and study completion. The total amount you may receive is up to $2565.00, assuming a 10-day inpatient stay. We will provide the compensation in 3 installments via checks at the visits indicated on your Payment Schedule. The amount you receive will be



prorated if you do not complete the entire study. This includes the backup subjects who are discharged from the unit before the flu challenge is given. We ask that you notify the Internal Revenue Service (IRS) of this income. A Form 1099-MISC (for miscellaneous income) will be mailed to you for you to report this compensation to the IRS. We will also provide you with parking vouchers or bus tokens, if appropriate.

STUDY FUNDING

NIH is funding this research study. This means that the University of Maryland, Baltimore (UMB) CVD is receiving payments from NIH to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from NIH for conducting this study.

CONFIDENTIALITY AND ACCESS TO RECORDS

Efforts will be made to limit your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include:

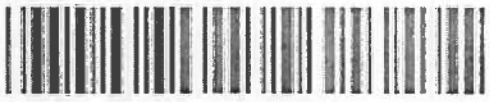
- the IRB and other representatives of this organization,
- federal government regulatory agencies,
- the U.S. Food and Drug Administration,
- the National Institutes of Health (NIH) and those contracted by the NIH, e.g. EMMES Corporation and Technical Resources International (TRI) pharmacovigilance and study monitoring groups
- auditing departments of the University of Maryland, Baltimore, and
- The University of Maryland, Baltimore Institutional Review Board (a committee that reviews and approves research studies) and other representatives of this organization.

To help protect your confidentiality, we will use ID numbers on research data. The data will be stored in locked cabinets and/or offices when not in use. Only research team members who are involved in the conduct, oversight or auditing of this study will have access to the research data.

Electronic data will be stored in password protected computers and websites. For this study, each blood and nose sample will be labeled with a barcode and a unique tracking number to protect our confidentiality. Personnel at the central storage and testing lab will not know your identity or the volunteer ID assigned to you for the study.

The data from the study may be published. However, you will not be identified by name. People designated from the institutions where the study is being conducted and people from the sponsor will be allowed to inspect sections of your medical and research records related to the study. Everyone using study information will work to keep your personal information confidential. Your personal information will not be given out unless required by law.

To help us protect your privacy, we have received a Certificate of Confidentiality from NIH. The certificate says that the investigators may not disclose research information that may



identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings, unless you have consented for this use. Research information protected by this certificate cannot be disclosed to anyone else who is not connected with the research unless:

- There is a law that requires disclosure (such as to report child abuse or communicable diseases, but not for legal proceedings).
- You have consented to the disclosure, including for your medical treatment.
- The research information is used for other scientific research, as allowed by federal regulations protecting research subjects.

As noted above, disclosure is required, however, for audit or program evaluation requested by the agency that is funding this project or for information that is required by the FDA. You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

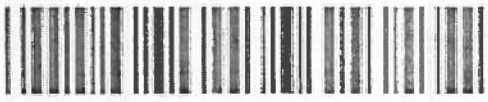
The University of Maryland, Baltimore generally requires that we document in your medical record chart that you are participating in this study. If you do not have a medical record in the UMMS system, then we will create one for you. The information included in the chart will provide contact information for the research team and information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

STUDY RESULTS

When the study results are available, after the study is completed (generally at least several months after your last visit), a summary of the study results will appear on http://www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time. Learning about study results can cause people to become upset, especially if the results are different from what you expected. If you have any questions or concerns about the results, please contact the PI, Dr. Kathleen Neuzil at 410-706-6156.

WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires University of Maryland, Baltimore to obtain your permission for the research team to access or create "protected health information" about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study.



Efforts will be made to limit your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the University of Maryland, Baltimore Institutional Review Board (IRB) and other representatives of this organization, federal government regulatory agencies, the US Food and Drug Administration, the National Institutes of Health (NIH) and those contracted by the NIH, e.g. the Emmes Corporation (data coordinating center), Technical Resources International (TRI) (pharmacovigilance group), and ICON. The monitors, auditors, the IRB, and the Food and Drug Administration will be granted direct access to your medical records for verification of the research procedures and date. By signing this document, you are authorizing this access.

You cannot participate in this study unless you permit us to use your protected health information. Your decision will not affect your right to medical care.

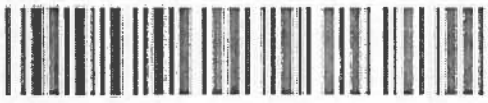
Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to Dr. Kathleen Neuzil at kneuzil@som.umaryland.edu. However, we may still use your health information that was collected before withdrawing your permission.

Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

RIGHT TO WITHDRAW

Your participation in this study is voluntary. You do not have to take part in this research. You are free to withdraw your consent at any time. However, we strongly discourage you from withdrawing after the flu virus has been given to you and before the required inpatient stay is completed. This is because leaving the unit when you may be infected with flu is a risk to you and to others. You could become sick with flu and we would not be there to follow you closely for signs of more serious illness. In addition, if you still have flu virus in your nose, you could spread that flu virus to others, including those who may be more likely than a healthy adult to get very sick from the flu virus. We will ask you to sign a form acknowledging these risks if you choose to leave the inpatient unit before we discharge you (Appendix A). We will encourage you to take one dose of the antiviral medication baloxavir. We will encourage you to avoid contact with anyone who could be at high risk of flu complications.

Not taking part in the study or stopping your participation in the study will involve no penalty or loss of benefits to which you are otherwise entitled. If you decide to stop taking part, or if you have questions, concerns, or complaints, or if you need to report a medical injury related to



the research, please contact the investigator, Dr. Kathleen Neuzil or her research team at 410-706-6156.

If you withdraw from this study, already collected data may not be removed from the study database. You will be asked whether the investigator can collect data from your routine medical care. If you agree, these data will be handled the same as research data.

You will be told of any significant new findings which develop during the study which may affect your willingness to participate in the study.

If you are an employee or student, your employment status or academic standing at UMB will not be affected by your participation or non-participation in this study.

If you decide to leave the study early, we will ask you to permit the study staff to contact you to follow up on any reactions you may have had and to collect blood samples, if possible.

CAN I BE REMOVED FROM THE RESEARCH?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include the following:

- Reasons related to you (for example, if you move to another city, do not agree to refrain from alcohol and drugs during the inpatient stay, or do not follow study-related directions).
- Reasons related to your health (for example, if you may be at risk for complications of flu due to a new medical condition).
- We have too many participants for the inpatient part of the study
- Because this entire study is stopped (the sponsor may stop this study at any time).
- If you do not later consent to any future changes that may be made to how this study is done.
- If you become pregnant.

The sponsor, the study doctor, or the Institutional Review Board (IRB) can also end the research study early. The study doctor will tell you about this and you will have the chance to ask questions if this were to happen.

UNIVERSITY STATEMENT CONCERNING RESEARCH RISKS

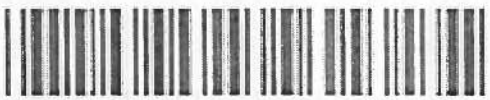
The University of Maryland, Baltimore (UMB) is committed to providing participants in its research the rights due them under State and federal law. You give up none of your legal rights by signing this consent form or by participating in the research project. This research has been reviewed and approved by the Institutional Review Board (IRB). Please call the Institutional Review Board (IRB) if you have questions about your rights as a research subject.

Participating in research may result in an injury, as explained above. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH or the Federal Government. If you suffer an injury directly related to your participation in this project, UMB and/or one of its affiliated institutions or health care groups will help you obtain medical treatment for the specific injury and provide referrals to other health care facilities, as appropriate. UMB and/or its affiliated institutions or health care groups will not provide you with financial compensation or reimbursement for the cost of care provided to treat a research-related injury or for other expenses arising from a research-related injury. The institution or group providing medical treatment will charge your insurance carrier, you, or any other party responsible for your treatment costs. If you incur uninsured medical costs, they are your responsibility. The study staff can give you more information about this if you have a study injury.

By signing this Consent Form, you are not giving up any legal rights. If this research project is conducted in a negligent manner and you are injured as a direct result, you may be able to recover the costs of care and other damages from the individuals or organizations responsible for your injury.

If you have questions, concerns, complaints, or believe you have been harmed through participation in this research study as a result of researcher negligence, you can contact members of the IRB or the Human Research Protections Office (HRPO) to ask questions, discuss problems or concerns, obtain information, or offer input about your rights as a research participant. The contact information for the IRB and the HRPO is:

University of Maryland Baltimore
Human Research Protections Office
620 W. Lexington Street, Second Floor
Baltimore, MD 21201
410-706-5037



Signing this consent indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

If you agree to participate in this study, please sign your name below.

_____
Participant's Printed Name

_____
Participant's Signature

Date: _____

_____
Investigator or Designee Obtaining Consent Signature

Date: _____ Time: _____

PID: _____

UNIVERSITY of MARYLAND BALTIMORE

Health Insurance Portability and Accountability Act (HIPAA)
AUTHORIZATION TO OBTAIN, USE AND DISCLOSE PROTECTED HEALTH INFORMATION FOR RESEARCH

Name of Study Participant:_____

Date of Birth: _____ **Medical Record Number:** _____

NAME OF THIS RESEARCH STUDY: A Controlled Human Infection Study of Influenza A/Bethesda/MM2/H1N1 Virus (A/California/04/2009/H1N1-like) in Healthy Subjects to Assess the Effect of Pre-Existing Immunity on Symptomatic Influenza Virus Infection

UMB IRB APPROVAL NUMBER: HP-00087487

RESEARCHER'S NAME: **KATHLEEN M. NEUZIL, MD, MPH**

RESEARCHER'S CONTACT INFORMATION:

Center for Vaccine Development and Global Health
University of Maryland School of Medicine (UMSOM)
685 West Baltimore Street, Room 480
Baltimore, Maryland 21201
Tel: (410) 706-6156; [redacted]

This research study will use health information that identifies you. If you agree to participate, this researcher will use just the health information listed below.

THE SPECIFIC HEALTH INFORMATION TO BE USED OR SHARED:

- Health-related information you have been asked to provide for the study during interviews and via questionnaires
- Results of medical tests, laboratory tests, research procedures carried out for the purpose of the study
- Medical records from another health care facility that may be needed to determine whether a side effect or other problem is related to the study
- Billing and payment information and the medical information required to justify it.

Federal laws require this researcher to protect the privacy of this health information. She will share it only with the people and groups described here.

PEOPLE AND ORGANIZATIONS WHO WILL USE OR SHARE THIS INFORMATION:

- Dr. Kathleen Neuzil and her research team, including the nursing, laboratory, and regulatory affairs staff at the Center for Vaccine Development and Global Health (CVD), and contracted affiliates of the CVD such as the Garcia Clinical Laboratory.
- The sponsor of the study, National Institute of Allergy and Infectious Diseases of the National Institutes of Health or its agents, such as data repositories or contract research organizations
- Federal and state agencies that have authority over the research, including the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and the Office of Human Research Protections

- University of Maryland Medical System (UMMS)
- Clinical staff not involved in the study who may become involved in your care if it is potentially relevant to treatment
- Organizations that will coordinate health care billing or compliance such as offices within UMSOM; the University of Maryland, Baltimore (UMB); University Physicians, Inc. (UPI) and the faculty practices of the UMB; and University of Maryland Medical System (UMMS)
- Your health insurer to pay for covered treatments

THIS AUTHORIZATION WILL NOT EXPIRE. BUT YOU CAN REVOKE IT AT ANY TIME.
To revoke this Authorization, send a letter to this researcher stating your decision. She will stop collecting health information about you. This researcher might not allow you to continue in this study. She can use or share health information already gathered.

ADDITIONAL INFORMATION:

- You can refuse to sign this form. If you do not sign it, you cannot participate in this study. This will not affect the care you receive at:
  - University Physicians, Inc. (UPI)
  - University of Maryland Medical System (UMMS)

  It will not cause any loss of benefits to which you are otherwise entitled.
- Sometimes, government agencies such as the Food and Drug Administration or the Department of Social Services request copies of health information. The law may require this researcher, the UMSOM, UPI, or UMMS to give it to them.
- This researcher will take reasonable steps to protect your health information. However, federal protection laws may not apply to people or groups outside the UMSOM, UMB, UPI, or UMMS.
- Except for certain special cases, you have the right to a copy of your health information created during this research study. You may have to wait until the study ends. Ask this researcher how to get a copy of this information from her.

My signature indicates that I authorize the use and sharing of my protected health information for the purposes described above. I also permit my doctors and other health care providers to share my protected health information with this researcher for the purposes described above.

Signature: _____ Date: _____

Name (printed) _____

Privacy Questions? Call the UMSOM Privacy Official (410-706-0337) with questions about your rights and protections under privacy rules.

Other Questions? Call the researcher named on this form with any other questions.