# Informed Consent

# Nasal Mucosal Immune Responses to Live Attenuated Influenza Virus (LAIV) in Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Phenotypes

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**Document Date** 12/13/2023

**University of North Carolina at Chapel Hill**
**Consent to Participate in a Research Study**
**Adult Participants**
**Consent Form Version Date:** _December 13, 2023_____
**IRB Study #** 21-0254
**Title of Study**: Nasal Mucosal Immune Responses to Live Attenuated Influenza Virus (LAIV) in Chronic Obstructive Pulmonary Disease (COPD) Exacerbation Phenotypes
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The purpose of this study is to understand how nasal inflammation after the nasal flu vaccine can help us learn about control of COPD. We are collecting samples from people with COPD and people without COPD (called "controls") for comparison.

You will be asked to first answer questions, have blood tests, and do breathing tests to see if you are eligible for the study. If so, we will then collect three different nose samples and a blood sample at the next visit. We will then give you the nasal flu vaccine. We will then ask you to return on days 1, 2, 3, 7 and 21 (or up to day 30 if needed for your schedule) after the nasal flu vaccine to collect nose and blood samples again. You will also be asked to answer some questions at each visit.

The main risks of this study are coughing and chest discomfort during breathing tests. One of the nasal samples has a low risk of nose bleeding or discomfort. Risk of taking blood samples are discomfort, bruising, or fainting. Mild flu-like symptoms are common in the 7 days following the nasal flu vaccine and may include cough, runny nose, sore throat, chills, sinusitis, and tiredness or weakness. It is possible (although a rare chance) that you could transmit the weakened flu virus to someone else if they have a weakened immune system. To reduce this risk, you can't be in the study if you will have contact with someone with weakened immune system for three weeks after the flu vaccine administration. There are no direct benefits to being in this study, but you may benefit from knowing that you are contributing to research and society.

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

**What are some general things you should know about research studies?**
You are being asked to take part in a research study. To join the study is voluntary.

You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

**What is the purpose of this study?**

People with the lung disease called chronic obstructive pulmonary disease, also called COPD, can have breathing flares (sometimes called "exacerbations"). The causes of breathing flares are not totally understood. The tissue in your nose is the target for many different infections. The purpose of this research study is to collect samples from your nose before and after we give you the nasal flu vaccine. We think this will help us learn about how the nose responses might be related to control of COPD. We can do experiments with cells from your nose, the fluid in your nose and from your blood to study how changes in nose inflammation makes breathing flares occur. The flu vaccine we are using (Flumist) is FDA-approved, but it is being used off-label in this study.

We plan on getting samples from people with COPD and from people without COPD (called "controls") for comparison.

You are asked to be in the study because you either have COPD or are willing to provide samples as a control without COPD.

**Are there any reasons you should not be in this study?**

You should not be in this study if you have used cigarettes or e-cigarettes in the last three months, use nasal steroid sprays, regularly use antibiotics such as azithromycin, have used oral prednisone in the last 30 days, have ever been hospitalized with COVID, have had nasal or sinus surgery or a history of regular nose bleeding, are on blood thinners or have a history of bleeding gums or easy bruising, or have a weakened immune system due to medications.

The nasal flu vaccine is called a live, attenuated vaccine. This means that the vaccine contains a weakened version of the flu virus. People with healthy immune systems do not get the flu from this vaccine. But if you have a weakened immune system from illness or medications, you should not be in this study. If you are not able to avoid contact with someone else with a weakened immune system for 3 weeks after receiving the vaccine, you should not be in this study.

**How many people will take part in this study?**
Approximately 40 people at University of North Carolina at Chapel Hill will take part in this study.

**How long will your part in this study last?**
If you join this study, you will be enrolled for up to 8 weeks.. The first visit (to see if you are able to participate and collect samples) should take no more than 3 hours. You will then be seen at a second visit to get nasal and blood samples, which should take 1 hour. You will then return for your nasal flu vaccine administration. That visit will take no more than 1.5 hours. You will then return on days 1, 2, 4, 7 and 21 (or up to day 30 if needed for your schedule) after the flu vaccine day to collect samples, with each visit lasting about one hour. We may use de-identified specimens from this study in future research without additional consent. Samples will be stored for as long as needed for that research.

**What will happen if you take part in the study?**

1. First visit: Screening Visit

The reason for this visit is to see if you are eligible for the study. This visit will last about three hours.

During this visit, you will:
- Be asked to review, sign and date the consent form. We will answer your questions about joining this research study.
- Answer questions about your medical history and current breathing symptoms.
- Have vital signs measured
- Have a brief physical exam by a research physician.
- Have about one tablespoons of blood drawn from a vein in your arm during this visit. We will use this blood to measure your blood counts and for HIV testing. These tests must be normal for you to join the study. You will be given the results of these tests.
- Women who are capable of becoming pregnant will have a urine pregnancy test. The result of this test must be negative for you to join the study.
- Be asked to perform breathing tests (spirometry) to measure your lung function.

  Spirometry measures how well you are able to breathe. During this test, you will wear a clip on your nose and blow air forcefully from your lungs. We will measure how much air comes out and how fast the air comes out. You will do this test before and after inhaling a medication (albuterol) that can help the breathing tubes to open up.

Based on these results, if you are eligible for the study and willing to be involved, you will be asked to return for the second visit within two weeks.

2. Second visit: Enrollment Visit

The reason for this visit is to collect your first nasal samples. This visit will last about one hour.

During this visit, you will:
- Have vital signs measured
- Answer questions about medical issues since your last visit
- You will be asked to give the following samples at this visit:

**Epithelial fluid lining**: This sample is collected by you spraying mild salt water mixture into your nose, then inserting thin filter paper into each nostril, and then placing nose clips on for two minutes. You will need to breathe through your mouth for the 2 minutes. After the 2 minutes the filter papers will be removed.

**Nasal lavage**: this involves having you spray a mild salt water solution into your nose repeatedly followed by blowing the return fluid from your nose into a cup.

**Nasal biopsy**: One of the study researchers who is trained will perform a biopsy procedure to retrieve a small cluster of cells from each of your nasal cavities. For the biopsy procedure, you will be seated comfortably in a straight-backed chair or reclining on an examination table with you tilting your head as far back as is comfortable A short, sterile plastic sampling device called a curette will be inserted into the inside of one side of your nose and the surface of your nasal cavity will be stroked several times for approximately 5 seconds in order to collect a small cluster of cells. This will be repeated on the other side using a fresh curette.

**Blood Draw:** We will draw blood from your vein. The most we will draw at any one time is 30 cc, which is roughly about 2 tablespoons. Genetic testing will not occur as part of the main study aims.

3. Third Visit: Nasal flu vaccine administration

The reason for this visit is to give you the nasal flu vaccine. This visit will last about an hour and a half.

During this visit, you will:
- Have vital signs measured
- Answer questions about medical issues since your last visit
- Answer questions about your current breathing and overall symptoms
- Women who are capable of becoming pregnant will have a urine pregnancy test. The result of this test must be negative for you to continue in the study.
- Given the nasal flu vaccine. The vaccine is a live but attenuated (weakened) virus that is sprayed into the nostrils. While sitting in an upright position, we will place the sprayer holding the vaccine just inside the nostril and spray the small amount of liquid (the vaccine) into one nostril. We will then repeat on the other side.

4. Fourth Visit: Day 1 Follow-Up Visit

The reason for this visit is to collect nasal and blood samples. This visit will last about an hour.

During this visit, you will:

- Have vital signs measured
- Answer questions about medical issues since your last visit
- Answer questions about your overall symptoms
- Have two of the nasal samples (epithelial lining fluid and lavage) and blood collected

5. Fifth Visit: Day 2 Follow-Up Visit
The reason for this visit is to collect nasal and blood samples. This visit will last about an hour.

During this visit, you will:
- Have vital signs measured
- Answer questions about medical issues since your last visit
- Answer questions about your overall symptoms
- Have two of the nasal samples (epithelial lining fluid and lavage) and blood collected

6. Sixth Visit: Day 3 Follow-Up Visit
The reason for this visit is to collect nasal and blood samples. This visit will last about an hour.

During this visit, you will:
- Have vital signs measured
- Answer questions about medical issues since your last visit
- Answer questions about your overall symptoms
- Have the three nasal samples and blood collected similar to your first visit

7. Seventh Visit: Day 7 Follow-Up Visit
The reason for this visit is to collect nasal and blood samples. This visit will last about an hour.

During this visit, you will:
- Have vital signs measured
- Answer questions about medical issues since your last visit
- Answer questions about your overall symptoms
- Have two of the nasal samples (epithelial lining fluid and lavage) and blood collected

8. Eight Visit: Day 21 Follow-Up Visit
The reason for this visit is to collect nasal and blood samples. This visit will last about an hour.

During this visit, you will:
- Have vital signs measured
- Answer questions about medical issues since your last visit
- Answer questions about your overall symptoms
- Have one nasal sample (nasal lavage) and blood collected

**What are the possible benefits from being in this study?**
Research is designed to benefit society by gaining new knowledge. You will not benefit personally from being in this research study.

**What are the possible risks or discomforts involved from being in this study?**

Breathing Tests (Spirometry):
Sometimes this can make the chest sore for a day or so. Rarely, people may become dizzy during the test. The test is done while you are sitting to decrease this risk. Also, a laboratory technician is present during the entire test to monitor how you are feeling. During the test, you will be given a medication albuterol. The common side effects of this medicine include fast heart rate or shakiness. On rare occasions (less than 5% of the time) it may cause nervousness, or headache at the doses used in this study. If you develop any of these problems, we will monitor you closely until the problem goes away (typically in 30 minutes). On rare occasions, albuterol may cause arrhythmias (the heart beats in an abnormal way) or low potassium: these side-effects are usually related to taking high doses of the medication and so are very unlikely to occur during this study.

Epithelial lining fluid:
This procedure can be annoying, and the papers could cause you to sneeze.

Nasal lavage:
There are no risks associated with nasal lavage.

Nasal biopsy:
This procedure can cause mild temporary bleeding from the nose. This can be treated if it occurs by squeezing the tip of the nose for 5-10 minutes. Nasal biopsy also is transiently painful. This procedure requires only a few seconds and you are free to excuse yourself from this portion of the study at any time.

Blood Draw:
You may experience pain during the insertion of the needle or bruising after the blood draw. You may also feel lightheaded when the blood is drawn.

Live attenuated influenza virus:
Mild flu-like symptoms including cough, runny nose, headache, sore throat, chills, sinus congestion, tiredness or weakness may occur in the 7 days after receiving the nasal flu vaccine. If this happens, you can take Tylenol to reduce these symptoms.

For the three weeks after you get the nasal vaccine, there is a small chance you could transmit the flu virus to someone who has a weakened immune system (from illness or medications). You should not be in this study if you are not able to avoid contact with anyone with a weakened immune system. You should avoid contact with individuals with a weakened immune system for three weeks after receiving the nasal flu vaccine.

Written Questions:
There are no physical risks related to filling out questionnaires. There is a chance of distress if answers to these questions are not kept private. To minimize this chance, all information is kept in locked files or rooms. Any electronic information is protected by passwords and can only be seen by doctors or nurses who are part of the study. You may get tired or bored when we are

asking you questions or you are completing questionnaires. You do not have to answer any question you do not want to answer.

There may be uncommon or previously unknown risks. You should report any problems to the researcher.

Women who are pregnant may not participate in this study. Therefore, women who are able to get pregnant must have a pregnancy test before taking part in this study and on the day of flu vaccine administration. For the pregnancy test, you will give a urine sample at the visit. You will be told the results of the pregnancy test. If the pregnancy test is positive, you will not be able to participate in the study. The pregnancy test will be paid for by the study. The FluMist vaccine we are giving in this study is not absorbed into the body following intranasal administration and use by the mother is not expected to result in fetal exposure to the drug.

**What if we learn about new findings or information during the study?**
You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

**Will I receive any other clinical results?**

Other clinically relevant results of this research will be communicated with you. These include the lab tests of your complete blood count and HIV testing tests done at screening. We will give you these results at the enrollment visit (or after they are resulted if you are not eligible for the study and therefore do not have an enrollment visit).

**How will information about you be protected?**
You will be assigned a study number, and that is the number that will be used on all study records and data, and this number is all that will be entered into the study databases. Information obtained from these studies will be kept in confidential research records and maintained in a database at the University of North Carolina at Chapel Hill. The worksheets that the study coordinators use will have your name and study number, but this information will stay in the study file which will be kept in the study coordinators office or other locked storage area in the research office. Only the study physicians, research technicians and coordinators will have access to the paper records. The lab results from nasal swab for COPD patients during a breathing flare will become part of your medical record at UNC Healthcare.

Participants will not be identified in any report or publication about this study. We may use de-identified data and/or specimens from this study in future research without additional consent. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

**What is a Certificate of Confidentiality?**

This research is covered by a Certificate of Confidentiality. With this Certificate, the researchers may not disclose or use information, documents or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings in the United States, for example, if there is a court subpoena, unless you have consented for this use.

The Certificate cannot be used to refuse a request for information from personnel of a federal or state agency that is sponsoring the study for auditing or evaluation purposes or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law, such as mandatory reporting requirements for child abuse or neglect, disabled adult abuse or neglect, communicable diseases, injuries caused by suspected criminal violence, cancer diagnosis or benign brain or central nervous system tumors or other mandatory reporting requirement under applicable law. The Certificate of Confidentiality will not be used if disclosure is for other scientific research, as allowed by federal regulations protecting research subjects or for any purpose you have consented to in this informed consent document.

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

By signing this informed consent document, you agree that some of the information generated by participating in this study and/or a copy of the consent form may be included in your medical record and that this information may be viewed by other physicians or caregivers who provide healthcare services to you. This will allow the doctors caring for you to know what study medications or tests you may be receiving as a part of the study and know how to take care of you if you have other health problems or needs during the study. Additionally, the information may be shared with your medical insurance plan if the research services provided are billed to your insurance. Under North Carolina law, confidentiality does not extend to certain communicable diseases, such as TB, HIV, hepatitis, or other illnesses that put others at risk. If the researchers become aware that subjects have such an illness, they are required to report it to state authorities.

You will be asked to sign a separate form ("HIPAA Authorization") to allow researchers to review your medical records.

**Will you receive results from research involving your specimens?**

Most research with your specimens is not expected to yield new information that would be meaningful to share with you personally. There are no plans to re-contact you or other subjects with information about research results. The use of your samples may result in commercial profit. You will not be compensated for the use of your samples other than what is described in this consent form.

**What will happen if you are injured by this research?**

All research involves a chance that something bad might happen to you. If you are hurt, become sick, or develop a reaction from something that was done as part of this study, the researcher will help you get medical care, but the University of North Carolina at Chapel Hill has not set aside funds to pay you for any such injuries, illnesses or reactions, or for the related medical care. Any costs for medical expenses will be billed to you or your insurance company. You may be responsible for any co-payments and your insurance may not cover the costs of study related injuries.

If you think you have been injured from taking part in this study, call the Principal Investigator at the phone number provided on this consent form. They will let you know what you should do.

By signing this form, you do not give up your right to seek payment or other rights if you are harmed as a result of being in this study.

**What if you want to stop before your part in the study is complete?**

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

If you withdraw or are withdrawn from this study all data collected up until the point of withdrawal will be retained, however no additional information will be collected unless you provide additional written permission for further data collection at the time of your withdrawal

**Will you receive anything for being in this study?**
You will be receiving payment for taking part in this study. Any payment provided for participation in this study may be subject to applicable tax withholding obligations,

| **Study visit** | **Amount** |
|---|---|
| Screening visit | $75 |
| Enrollment visit | $75 |
| Vaccine administration visit | $75 |
| 5 follow-up study visits | $75 per visit (for a total of $375) |

You will also receive an additional $75 for completing all study visits.

Your name, address, and U.S. taxpayer identification number (SSN or ITIN) are required to process payments and/or to report taxable income to the IRS. You must complete a W-9 (for U.S. persons) or W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents (for non-resident aliens) in order to receive payment for participation.

U.S. person participants must complete Form W-9 in order to receive payment for participation. If payment by UNC equals or exceeds $600 per calendar year for U.S. persons,

UNC will report the amount to the Internal Revenue Service on Form 1099. Nonresident alien participants must complete Form W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents in order to receive payment for participation. Payments to nonresident alien participants may be subject to tax withholding and are generally reported to the Internal Revenue Service on Form 1042-S. This information will not be linked to any of the study data and will only be used for payment purposes.

If you do not provide your SSN or ITIN, or complete the appropriate documentation noted above, we cannot issue you a payment for participation. However, you may still choose to participate in this study

**Will it cost you anything to be in this study?**

It will not cost you anything to be in this study. Parking is free at the Eastowne Medical Office Building, where research visits occur. Therefore, we do not compensate for costs related to parking. In the event that parking charges do occur (due to change in policy), you will be reimbursed for parking.

**Who is sponsoring this study?**

This research is funded by the National Institutes of Health. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

**What if you have questions about this study?**

You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

A description of this clinical trial will be available on 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.

**What if you have questions about your rights as a research participant?**

All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

**Participant's Agreement**:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____
Signature of Research Participant

_____
Date

_____
Printed Name of Research Participant

_____
Signature of Research Team Member Obtaining Consent

_____
Date

_____
Printed Name of Research Team Member Obtaining Consent

_____
Signature of Witness if applicable; e.g. literacy issues, visually impaired, physically unable to sign, witness/interpreter for non-English speaking participants using the short form)

_____
Date

_____
Printed Name of Witness