University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants
Consent Form Version Date: February 14, 2018
IRB Study # 17-2275
Title of Study: In-vivo effects of E-cigarette aerosol on innate lung host defense
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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?
The purpose of this research study is to compare how mucus clears from the lungs after the use of an e-cigarette containing a particular flavor type, called cinnamaldehyde (CA) and after the use of an e-cigarette without the cinnamaldehyde flavor. We will compare both of these to how the mucus clears in healthy people who don't smoke anything.

Are there any reasons you should not be in this study?
You should not be in this study if you smoke anything besides e-cigarettes, if you have lung disease, if you are pregnant or planning to become pregnant in the immediate future, or if you have a history of exposure to higher than normal levels of radiation exposure in the past year. We will ask you about your radiation exposure, including any x-rays you've had done or if you

are exposed at work or school to be sure you don't have too much additional exposure by participating in this study.

How many people will take part in this study?
There will be approximately 44 people in this research study.

How long will your part in this study last?
There will be 3 visits for non-smokers and 6 visits for e-cig users. The 3 visits should be completed within about 2 weeks, the 6 should be completed in no more than two months. For everyone,

- The screening visit will take about 2 hours
- The baseline visit will take about 4 hours
- You will return in 24 hours for about an hour and a half.

At this point, if you do not use and e-cig, your will have completed the study.

For e-cig users:

- The training for the vape device that we use will take about an hour. We can do this when you finish with the 24 hour follow up, or you can come in on a different day.

Then you will start the vaping sessions.

- The first day of the vaping session will last about 4 ½ hours
- You will return 24 hours later, and this visit will last about 1 ½ hours.
- Two to three weeks later, you will repeat these 2 visits, with the first day lasting 4 14 hours and the 24 hour follow up lasting 1 ½ hours. When this visit is complete, you will have completed the study.

What will happen if you take part in the study?
You will come to the lab for an initial screening visit. At this visit, you will have an opportunity to read the consent form, and the study will be explained to you. We will answer all of your questions, and be sure you understand what is required to participate in this study.

Once you have agreed, we will:

- Collect your medical history from you, including your medications and information about any x-rays or CT scans you have had in the past year, or if you have any work exposure to radiation
- Collect urine to measure byproducts of nicotine
- Do a urine pregnancy test for all women, and it must be negative

- Measure your vital signs, including your heart rate, respiratory rate, blood pressure, temperature and the oxygen level in your blood with a finger probe. We only measure your temperature at the beginning of the study day
- We will listen to your chest with a stethoscope
- You will do a lung function test, called spirometry. We will coach you through this test, but you will take a breath in as deep as you can, and blow it out as hard and as fast as you can. You will repeat it several times.
- You will then undergo a sputum induction. You will inhale a heavy mist of salt water, at concentrations higher than the concentration of salt normally in your body. We will ask you to cough up a sample of sputum (phlegm) after you breathe in the salt water, and we'll instruct you on what you should do to give us the best possible sample. You will inhale 3 levels of the salt solution, and we will do a breathing test after each level to monitor your lung function.
- Once you complete the sputum induction, we will check your vital signs again
- You will be discharged home with contact information for a study physician.
- If you are an e-cig user, you will be sent home with a diary to collect your vaping sessions for the entire duration of the study.

The sputum samples allow us to better understand cells in the fluid of the lungs of people who don't vape, compared to people who do vape, including the different e-liquids. Please be aware that not everyone is able to produce an adequate sample (the number and type of cells we see under the microscope) and if your sample is not adequate, you will not be able to continue. It will take about 24 hours before we have the results.

If your sputum sample is acceptable, you will asked to return to the study lab for the baseline session. We will ask you to refrain from vaping for 12 hours before this visit. On arrival,

- We will ask about any changes in your health, your medications, or if you've had any x-rays since your last visit.
- We will collect urine for a pregnancy test.
- We will measure your vital signs.

Then, you will have a baseline Mucociliary Clearance Scan (MCC). You will then be seated in front of a gamma camera, which is a device for measuring radioactivity.

- First, a measurement of background radioactivity will be made for 15 minutes. We will then place a source of Cobalt 57 in front of your chest for 5 minutes to obtain a transmission scan of your lungs. This scan will identify various regions of your lungs to help the researchers analyze data from the gamma camera scan (described below).
- Next, you will be escorted into another room where you will inhale an aerosol of sulfur colloid labeled with the radioactive material, Technetium 99m. You will inhale the

aerosol according to a prescribed breathing pattern that you will practice prior to aerosol inhalation. Aerosol inhalation will take about 5 minutes.

- After inhaling the aerosol, you will then be seated in front of the gamma camera again for a measurement of radioactivity in your lungs. You will remain seated in front of the camera for a period of 120 minutes. During this time you will be allowed periodic breaks from sitting. The gamma camera will measure the rate that secretions clear from your lungs (mucociliary clearance rate).

At the end of the MCC, you will undergo a sputum induction just like you did on the screening day.

Approximately 24 hours following the aerosol inhalation, you will return for a half-hour scan of residual radioactivity in the lung.

- You will sit continuously in front of the gamma camera for 30 minutes.
- Then we'll measure your vital signs, and listen to your chest.
- You will have another sputum induction
- We will check your vital signs once more

If you are not an e-cig user, your participation is complete at this point.

If you use e-cigarettes, we will introduce you to the device that we will use for the study, and instruct you in the proper technique. We use an eVic™ Supreme, and we will provide the e-liquids for the vaping sessions. You will be asked to follow a laboratory-based protocol involving three, 10-minute paced vaping segments (2 puffs/minute). This device allows manual control and recording of the vapor settings (voltage, wattage, puff volume, and puff frequency), using the myVapors™ software. This visit can be done either at the end of the sputum induction, or at anytime before your next visit, but you must refrain from vaping for 12 hours before the visit.

You will be asked to continue the diary, and we will ask you how much nicotine is in the e-liquid you currently use. It will be important for the study for you to maintain a consistent vaping pattern throughout the study. After we collect your vital signs,

You will return to the lab 2-3 weeks later for your first study vaping session, and you must refrain from vaping for 12 hours before this session. You will receive either the CA-containing flavor, or the flavor without the CA, at this session. The order in which you receive the e-liquid is randomized, much like flipping a coin.

- We will update your medical history, including any changes in your medications or any new x-rays
- Women will have a urine pregnancy test done

- We then will check your vital signs
- You will do a lung function test
- Next, you will vape with the randomized e-liquid, either with or without CA, using the device you used with your last visit.
- Ten minutes after you complete the vaping session, you will undergo a MCC scan for 2 hours, just like before.
- After the scan we will collect your vital signs
- You will do a lung function test
- And you will undergo an induced sputum.
- Your vital signs will be collected again prior to discharge.

You will return the next day for a 24-hour follow up scan

- Please return your diary at this visit.
- We will collect your vital signs
- You will do a lung function test
- You will undergo sputum induction.
- Vital signs collection will be collected again prior to discharge.
- You will be reminded to continue your diary.

There will a 2-3 week washout, and you will return to repeat the session, vaping the e-liquid that you were randomized to vape for this session.

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?

You are only being asked to participate in the e-cigarette part of the study if you are already using e-cigarettes, so the risk should be no more than what you experience outside of the study.

The lung function test makes some people a little dizzy, or "light-headed". You will sit in a non-rolling chair during this test. The inhalation of the salt solution commonly causes coughing. This solution has a salty taste. Some patients also experience throat irritation, nausea, or wheezing. We have an albuterol inhaler to treat you if your lung function drops and does not come back quickly, or if you wheeze.

The lung clearance studies all involve exposure to some radiation. Since radiation can be especially harmful to a developing fetus, it is important that pregnancy be avoided during this study by using effective birth control measures (either hormonal contraceptives, like birth control pills; or a barrier method, like condoms). If you are participating as a vaper (3 MCC studies) the radiation dose you will receive in this study is 133 mRems. If you are participating as a

nonvaping/nonsmoking control (1 MCC study) the radiation dose you receive will be 44mRems. Both are less than the natural environmental radiation that you receive every year (300 mrem). The risk from the radiation dose received from this procedure is too small to be detected. The radiation exposure described here is what you will get from this research study only. It does not include any exposure you may have received or will receive from other tests outside this study that are a part of your medical care. You must inform one of the investigators if you have had any x-rays or other radiation exposure within the past year so that we do not exceed the yearly dose limits. If you wish, Dr. Bennett will provide you with additional information and answer any questions you may have. If desired, additional information can be obtained from Marija Ivanovic, Ph.D, Chairman of the Radiation Safety Subcommittee of UNC Hospitals at 919-843-0717. Although it is best to avoid radiation exposure, this is a small amount of radiation and is considered acceptable to experience on a limited basis. You should take this information into consideration when agreeing to participate in this study and any future studies. In addition, there may be uncommon or previously unknown risks that might occur. You should report any problems to the researchers.

This study is approved for three Tc99m SC scans and two Co57 transmission scans with a total dose of 133 rem (equivalent to exposure from background radiation in one year).

Pregnancy tests will be done on all females who might be able to get pregnant at the start of the study. The cost of the pregnancy test is covered by the study.

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.

How will information about you be protected?

Your information will stay with either the study coordinator or investigator. The data and samples will have your study number on them, which the research team can link to you, but only people who need to know who you are to do their jobs will have access to that information. Paper files are kept in an office which is locked after hours.

Participants will not be identified in any report or publication about this study. 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?

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose

information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family 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.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances. This could happen if you require medical treatment for any medical problems you might have related to the research.

What will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. This may include the risk of personal injury. In spite of all safety measures, you might develop a reaction or injury from being in this study. If such problems occur, the researchers will help you get medical care, but any costs for the medical care will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill has not set aside funds to pay you for any such reactions or injuries, or for the related medical care. You do not give up any of your legal rights by signing this form.

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.

Will you receive anything for being in this study?

You will be receiving up to $225 for taking part in this study, if you are a non-smoker. If you are an e-cig user, you will receive up to $750. This includes $50 for the screening visit, $150 for each MCC and sputum session, and $50 for vape training time, and $25 for keeping the diary. If you drop out of the study, or if we take you out for medical reasons, or if you do not produce an adequate sputum sample, we will pay you for visits you attend. We will give you parking coupons to cover the cost of parking in any UNC Hospitals lot for time you spend doing this study.

Your name, address, and social security number (SSN) are required to process payments and/or to report taxable income to the IRS. You will be asked to sign a separate Social Security Number Collection form. If you do not provide your SSN (or ITIN), 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.

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