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PARTICIPANT CONSENT FORM

Title of Study: 'Cardiopulmonary complications of electronic cigarettes'

Principal Investigator:	**Dr. Michael Stickland**	**Ph: 780-492-3995**
Research/Study Coordinator:	**Desi Fuhr**	**Ph: 780-492-1121**

Why am I being asked to take part in this research study?
You have been invited to participate because you meet the eligibility criteria for one of the study groups. Depending on your product use, you may be enrolled as:

- A control participant (you do not use an electronic nicotine delivery system (ENDS), smoke cigarettes, or smoke cannabis); or
- An ENDS user; or
- A cannabis smoker; or
- An ENDS user and cannabis smoker.

NOTE: ENDS include e-cigarettes, vapes, vaporizers, and vape pens and include any substance (nicotine, cannabis, CBD, or other types).

This study will not involve any medications for experimental purposes.

This form contains information about the study. Before you read it, a member of the study team will explain the study to you in detail. You are free to ask questions if there is anything you do not understand. You will be given a copy of this form for your records.

What is the reason for doing the study?
Electronic nicotine delivery systems (ENDS), including e-cigarettes, vapes, and vape pens, and cannabis smoking have become increasingly popular with both adolescent and adult Canadians, but the long-term health impacts remain unknown. Recent evidence shows that ENDS use may reduce a person's ability to exercise, increase shortness of breath, and make breathing less efficient during exercise. Some studies also suggest that ENDS use affects how well blood flows through the lungs and how effectively oxygen moves from the lungs into the bloodstream. However, we do not yet fully understand why these changes may occur with ENDS use.

The lungs move oxygen into the blood and remove carbon dioxide, which depends on lung blood vessel function. During exercise, the body needs more oxygen, so the lungs and heart must work harder, and blood vessels in the lungs normally expand to carry

more blood. If the blood vessels are not working properly, a person may have reduced exercise ability or become short of breath more quickly.

In this study, we will measure how well the lungs transfer oxygen both at rest and during certain controlled challenges, such as exercise and brief changes in lower body pressure. These challenges temporarily change blood flow and allow us to see how the heart and lungs respond under stress. Ultimately, this research may help us detect early changes in lung blood vessel health that are not noticeable at rest.

What will happen in the study?
This study consists of 6 visits ranging from 1 hour to ~4 hours per visit (~12 hours total). 5 visits will take place at the Clinical Physiology Laboratory located in the Clinical Sciences Building, and 1 visit will take place at MIC Medical Imaging – Century Park. You can take breaks as needed during all study visits.

For all visits, we ask that you refrain from alcohol for 24 hours, heavy exercise for 12 hours, as well as from consuming food and caffeine for 2 hours prior. We also ask that you refrain from using ENDS for at least 6 hours prior to visits 2-6.

Visit 1: Screening, lung and exercise tests (3-4 hours).
This visit involves the following procedures:

1. **Blood Collection:** 15 to 30 mins
   A blood sample will be collected for analysis. Approximately 2-5 teaspoons (12-25mL) of blood will be collected.

2. **Questionnaires:** approximately 40 minutes
   You will complete questionnaires on an online survey system on a tablet. The questionnaires will ask about your use of electronic nicotine delivery systems (ENDS), e-cigarettes, and traditional cigarettes, as well as any respiratory symptoms you may be experiencing. These questionnaires will assist us in monitoring changes in product usage over time and assessing the severity of symptoms.

   - Assessment of ENDS Use Questionnaire: approximately 5 minutes
     You will be asked to fill out a detailed questionnaire about your electronic nicotine delivery systems (ENDS), e-cigarette and cigarette habits at different times during the study. This helps us track any changes in how you use these products over time. The questionnaire will cover things like:
       - What types of e-liquids you use, how strong they are, and how much you use them;
       - The flavors and brands of e-liquids you prefer;
       - What kind of devices you use and how often;
       - How many times you puff on your e-cigarette each day
       - How long you have been using e-cigarettes.

     We will also ask about your past and current habits with smoking regular

cigarettes, using cannabis, drinking alcohol, and using illegal drugs at each time point. We will also ask you if you have been sick or experienced shortness of breath in the past 3 months.

- St. George's Respiratory Questionnaire (SGRQ): approximately 15 minutes
  This questionnaire consists of 50 questions about how your breathing issues affect your ability to do activities in your everyday life. Most questions are true or false (e.g. coughing hurts, true or false?).

- COPD Assessment Test (CAT): approximately 5 minutes
  This questionnaire consists of 8 questions in which you rate how affected you are by different breathing symptoms on a scale of 1 to 5.

- International Physical Activity Questionnaire (IPAQ): approximately 5 minutes
  This questionnaire consists of 7 questions in which you describe your physical activity levels.

- Modified Medical Research Council (mMRC) Dyspnea (Shortness of Breath) Score: approximately 3 minutes
  You will be asked to provide a score between 0 and 4 to assess the degree of disability due to shortness of breath.

- McMaster Cough Severity Questionnaire (MCSQ): approximately 5 minutes
  You will be asked 8 questions on how badly your cough affects you.

3. **Pulmonary Function Test:**
   You will undergo a Pulmonary Function Test, which involves breathing into a tube to assess how well your lungs work. The test will measure blockages in your air passages, lung volumes, and the lung's ability to transfer oxygen to the blood.

   - Spirometry, Lung Volumes, & Diffusion Capacity (approximately less than one hour) **–** This test will require you to breathe in and out forcefully into a small tube. This test measures the extent of obstruction in your air passages, the lung volumes, and the lung's ability to transfer oxygen to the blood. On each day of testing the test will be repeated at least three times to make sure an accurate result is obtained. The test will take less than one hour in total.

   - Oscillometry (approximately 30 minutes): This is a simple way for the doctor to measure your lung function. Oscillometry uses sound waves to measure if the airways are blocked at all because of asthma or other conditions that affect breathing.

4. **Cardio-Pulmonary Exercise Test (CPET):** approximately 20 mins
   You will undergo a Cardiopulmonary Exercise Test (CPET) on a stationary bike. First, you will rest for 6 minutes, then pedal for 1 minute without any added weight on the bike to warm up. After that, the resistance will slowly increase, and you will pedal until

you can't continue.

5. **Activity Monitoring:** worn at home for 7 days
   You will be given an activity monitor (Fitbit) to wear on the wrist continuously for 7 days to measure daily physical activity. The device should be worn at all times, except when charging, or when removal is required for activities such as bathing or contact sports.

   A charger will be provided. After the 7-day period, you will be asked to return the device to the lab. If needed, a pre-paid, pre-addressed mailing package will be provided for its return.

Visit 2: Exercise and Blood Vessel Function (~2 hours).
During this visit you will do several 6-second breath-holds at rest and during easy to very hard exercise on the same stationary bike used in your previous visit. The breath-holds let us look at your lung blood vessel function. This day will start with coaching and practice on how to perform these breath-holds.

There will be up to 6 stages of rest and exercise, with 2 breath-holds performed during each stage. We will collect a fingertip prick blood sample once during each stage, for up to 6 poke samples in total. We will measure your heart rate, blood pressure, and oxygen saturation throughout. If you experience any discomfort, you may stop the test at any time by informing a member of the research team.

Visit 3: Blood Volume Movement and Blood Vessel Function (~2 hours).
During this visit, you will do the same breath-holds as visit 2. You will do the breath-holds while lying on your back in the lower body pressure chamber. A lower body pressure chamber is a device that covers your lower body from your hips to your toes and gently applies either positive pressure (LBPP) by pushing blood from your legs towards your chest, or negative pressure (LNBP) by pulling blood towards your legs. Your lower body will be sealed within the chamber via a compression skirt to prevent any air leakage from the inside of the chamber. The pressure chamber allows us to safely study how the blood vessels in your lungs respond to changes in blood flow. At each pressure level, you will do 2 breath-holds.

We will also measure your heart rate, blood pressure, vein pressure, and oxygen saturation throughout. A fingertip prick blood sample will be collected twice during your visit, once at the beginning and another time towards the end of the test. You may take breaks as needed during the test and may stop the procedure at any time by informing a member of the research team.

1. Resting breath-holds: First, you will perform 2 breath-holds lying down in the lower body pressure chamber under normal room pressures.

2. LBNP/LBPP breath-holds: Next, while remaining lying down in the lower body pressure chamber, you will perform 2 breath-holds at each stage of LBNP or

LBPP. The LBPP/LBNP stages range between +40 mmHg and −80mmHg. These pressure changes temporarily alter the amount of blood returning to your heart, similar to the changes that occur naturally when you stand up or lie with your feet above your head. The pressure levels used in this test are designed to produce mild, temporary changes in blood flow and blood pressure. You may experience sensations such as lightheadedness, dizziness, or discomfort during the pressure changes. The research team will monitor you throughout the test, and you may take a break or stop the test at any time if you feel uncomfortable. The LBNP/LBPP pressures will be measured by a digital pressure monitor attached to the chamber. This allows the research team to monitor the pressure and adjust it to the desired level using a vacuum pump.

Visit 4: Ultrasound Imaging (~2 hours).
During this visit, you will complete the same exercise as visit 2 and the same pressure challenge as visit 3. During each stage of exercise and pressure, a trained professional will use an ultrasound probe and gel on your chest to take pictures of your heart. The ultrasound uses sound waves to create images of your heart and is painless. These images help us see how your heart pumps and responds to exercise and changes in blood movement. You will have the opportunity to rest between stages.

Visit 5: Blood Volume Measurement (~2 hours).
During this visit, a trained technician will insert an IV catheter into your forearm. You will then do a carbon monoxide rebreathe test so we can estimate your blood volume. A small, controlled amount of carbon monoxide is used as a tracer because it mixes with the blood during the rebreathing test. The change in concentration of carbon monoxide in the rebreathed gas is used to estimate your blood volume. Blood volume is an important part of the cardiovascular system because blood carries oxygen throughout your body. The use of carbon monoxide is the gold standard technique for estimating blood volume.

A small volume of carbon monoxide will be mixed with 100% oxygen in a sealed bag. You will breathe in the contents of this bag, hold your breath for 10 seconds, and continue to rebreathe the same gas for two minutes. You will then lie still for eight minutes. We will take a blood sample from your IV before the rebreathe and a second sample eight minutes after the rebreathe test.

Visit 6: Chest Computed Tomography (CT) Scan (30-60 mins).
You will have a CT scan as part of the study. The CT scan will take cross-sectional images (slices) of your chest to allow us to look at the blood vessels in your lungs and measure their volume. A CT scanner looks like a large donut with a narrow table in the middle. While you are lying on the table, the table will slowly move through the “donut-hole” taking pictures of your chest.

What are the risks and discomforts?
Participation in this study may involve some added risks or discomforts. Precautions and screenings will be in place to minimize these risks. These risks include:

Questionnaires: You may feel uncomfortable answering some of the questions. You do not have to answer any question that you do not want to answer. Note that studies involving humans now routinely collect information on race and ethnic origin as well as other characteristics of individuals because these characteristics may influence how people respond to different drugs such as tobacco and cannabis. Providing information on your race or ethnic origin is voluntary.

Pulmonary Function Tests: Lung function tests may make you feel short of breath or dizzy. If you feel this way during the test, please let the technician or study coordinator know. If you experience any discomfort, you may stop the test at any time by informing a member of the research team. Some potential harms and discomforts associated with this procedure include:

Discomfort during Testing: Some individuals may experience discomfort during the procedure, particularly if they are sensitive to the sensation of breathing through a device or if they have respiratory conditions that make breathing difficult.

Nasal Discomfort/General Discomfort: the procedures often involve breathing through a mouthpiece or a nose clip, which may cause nasal discomfort or irritation. Some individuals may feel uncomfortable or anxious when using certain devices or being in close proximity to equipment. To minimize discomfort, the research team will ensure that all equipment is fitted properly, explain each procedure before it begins, and allow you to take breaks or stop the procedure at any time.

Cardio-Pulmonary Exercise Test (CPET): During the CPET, you will perform exercise that gradually becomes more difficult until you reach your maximum effort or can no longer continue. This is a maximal exercise test designed to assess how your heart, lungs, and muscles respond to intense exercise.

CPET is generally considered safe and well-tolerated. However, there are potential risks and discomforts that merit consideration. CPET involves physical activity that may stress the heart, especially if you have heart problems. This could lead to irregular heartbeats, heart muscle issues, or even a heart attack. There is a very small risk of a serious cardiac event, such as an arrhythmia, heart attack or death, associated with heavy exercise in healthy people (less than 9 in 10,000). If you have conditions like COPD or asthma, CPET might worsen your breathing symptoms, causing difficulty breathing, wheezing, or even breathing failure in extreme cases. The exercise part of CPET could strain muscles or joints, especially if you already have muscle or joint problems or if you're not used to physical activity. Though rare, some people might faint or collapse during or after CPET, particularly if they have certain underlying conditions.

Throughout the test, you will be closely monitored by qualified research staff who are trained and certified in first aid and emergency response. The research team will stop the test immediately if there are any signs that it is unsafe for you to continue. You may stop the test at any time if you feel unable or unwilling to continue. Should you experience any symptoms during or following your test, a trained researcher will stay with you until you

feel better. In the unlikely event of a medical emergency, trained staff will provide immediate first aid and will contact emergency medical services if required. Emergency equipment, including an automated external defibrillator, and procedures are in place to ensure your safety.

If you have any questions or experience any unexpected symptoms after your study visit, please contact the research team using the contact information provided at the beginning of this consent form. If your symptoms are severe or occur outside of business hours, please call 911 or go to the nearest emergency department and notify us as soon as reasonably possible.

Blood Sampling: Pain, bruising, or in very rare cases, an infection may occur at the site of needle puncture. To minimize these risks, blood will be drawn by trained and experienced technicians using sterile, single-use equipment and standard infection-control procedures. The puncture site will be cleaned prior to needle insertion, and pressure will be applied after sampling to reduce bruising.

CT Scan: This procedure exposes you to radiation. While you may be exposed to greater radiation than usual, the risk that you experience side effects due to radiation is very low. You will be asked to perform CT no more than once per year (or longer), for up to 2 CT scans in total. The dose of radiation that participants will receive from a CT scan is estimated at below 3.0 milli-Sieverts (mSv). We are exposed to radiation from natural sources in our environment all the time. It takes 1 year of exposure for the average person to receive an effective dose of about 3 milli-Sieverts from naturally occurring radioactive materials. These natural "background" doses vary from area to area.

Lower-body Negative Pressure: There is a small risk of brief lightheadedness and fainting during lower-body negative pressure. However, we will monitor your blood pressure and heart rate, and we will stop the test if we see your blood pressure drop. We also ask that you tell us if you feel light-headed, sweaty, or have “tunnel” vision. If you feel any of these symptoms, we will stop the test, and you should feel better right away.

Finger Prick Blood Sample: You may feel minor discomfort as your finger is pricked.

Ultrasound Imaging: There are no known risks to ultrasound imaging of the heart or blood vessels. However, you may feel some discomfort during the heart imaging as the ultrasound probe will be pressed against your chest. If an abnormal finding is discovered, we will inform you of this, and one of the study physicians will follow up with you regarding the results.

Catheters: A trained technician will insert your catheters and will stay in the room for the whole trial to make sure no problems arise. Risks of a catheter in your vein include bruising, clot formation, or infection. These risks are rare (less than 1%) in participants who have the catheter in place for less than 5 hours. You may feel some discomfort when we insert the catheter. We will lower all the risks by having a trained professional perform the procedure under sterile conditions.

Risks related to intravenous (IV) lines include bleeding from the catheter site and infection of the catheter site. These risks are rare (less than 1%). To lower these risks, a trained technician will place the IV with good technique and sterile precautions. We will clean the skin site with an antiseptic, and we will use sterile, commercially available catheters. We will use full sterile precautions for blood sampling from your IV as well. Our blood sampling uses a closed system, which is the same as what is often used in hospitals.

Carbon Monoxide Rebreathe: The carbon monoxide rebreathe includes breathing more carbon monoxide than you would be exposed to in day-to-day life. In large doses carbon monoxide can be toxic because it competes with oxygen in the blood and could cause you to get too little oxygen around your body. Because of this risk, we have several safety strategies in place. First, you will get a known dose of carbon monoxide that has been shown to be safe in past research. The dose you will get will cause ~6% carbon monoxide saturation in your blood and you should not feel any symptoms from this dose. The dose will increase your carbon monoxide saturation like a regular smoker. Other research has shown that up to ~20% carbon monoxide saturation is not harmful. We will measure your carbon monoxide saturation using a finger clamp. We will stop the protocol if your carbon monoxide saturation goes above 12%. We will also stop the protocol if you or the research team see any symptoms of carbon monoxide poisoning. Symptoms to look out for include headache, nausea, or cognitive impairment. We also have 100% oxygen available. Breathing pure oxygen will make sure your body gets enough oxygen. It will also speed up carbon monoxide removal from your blood. The carbon monoxide level in your blood will gradually decrease over the next several hours. Most participants do not experience any symptoms at the dose used in this study. If you experience any symptoms, they should happen during the protocol and resolve as the carbon monoxide is cleared from your body.

If you have any questions or experience any unexpected symptoms after your study visit, please contact the research team using the contact information provided at the beginning of this consent form. If your symptoms are severe or occur outside of business hours, please call 911 or go to the nearest emergency department.

Pregnancy: The CT scan may not be safe during pregnancy. If you are a woman of childbearing potential not using contraception, you will be asked to have a negative urine pregnancy test before starting the study. We will provide a test for you. Acceptable contraception includes tubal ligation, oral contraceptive, barrier methods (intrauterine device, diaphragm, female condom, male condom). Abstinence is an acceptable form of contraception. But, if you practice abstinence it is important to use another method of birth control if you become sexually active during the study.

Blood Pressure: There are no risks associated with the use of finger or arm cuffs to examine blood pressure. Some individuals may feel discomfort and numbness in the fingertip during long testing sessions. This goes away immediately upon cuff removal.

Disclosure Risks: Some risk to privacy always exists when personal health information is shared, however, all your information used in this study will be handled and stored securely and nothing that identifies you will be released. Any personal information collected will be protected and kept separate from coded study data.

Incidental Findings: It is possible that the study tests may discover a finding that the researchers were not looking for. The study tests will be reviewed by a qualified investigator and these findings will be reported to you. If the findings are thought to affect your health, the study team will contact your family physician with your permission and assist with follow-up. No information from this study will become part of your health record. However, if an abnormality is detected and further follow-up is required, then this information may become part of your health record.

Other Risks: There are no risks associated with recording heart rate or oxygen saturation.

What are the benefits to me?
There will be no direct benefit to you from participating in this study. This study will look at how the use of ENDS and cannabis impact the blood vessels in the lungs. We hope that future patients may benefit from this knowledge.

What happens if I am injured because of this research?
In the case of research-related side effects or injury, you will be referred for appropriate medical care.

What are the rights of participants in a research study?
You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study. Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form, you do not give up any of your legal rights against the study doctor, sponsor or involved institutions for compensation, nor does this form relieve the study doctor, sponsor or their agents of their legal and professional responsibilities.

Do I have to take part in the study?
Being in this study is your choice. If you decide to be in the study, you can change your mind and stop being in the study at any time, and it will in no way affect the care or treatment that you are entitled to.

What will it cost me to participate?
Participating in this study will not cost you anything. You will be reimbursed for parking or transit costs associated with each study visit.

Will I be paid to be in the research?
You will not be paid for participating in this study. However, you will be reimbursed for parking or transit expenses, and as a thank you for your time and effort, you will receive $50 for each study visit.

Privacy and Confidentiality
During this study we will be collecting information (or "study data") about you. We will use the data to help answer research questions and we will share (or "disclose") your information with others such as other researchers.

Below we describe in more detail how your data will be collected, stored, used and disclosed.

What data will we be collecting?
During this study we will be collecting data about you. Examples of the types of data we may collect include your name, ethnic background, date of birth, age, health history and medications. We will only look for and collect the information that we need to do the research. We will get this information by asking you questions and doing the tests outlined in this form.

How will the study data be stored?
The study data we collect which will include your name will be securely stored during and after the study. At the University of Alberta, regulations say we have to keep the study data stored for at least 5 years after the end of the study.

The study staff will not release your name to anyone unless required by law.

How will the study data be used?
Your study data will be coded (with a number) so that it no longer contains your name or anything else that could identify you. Only investigators will be able to link your coded study data to you. The risk to your privacy, then, should be very small.

When the study is done, the investigators may place your coded study data into a secure database. The coded data may then be used to answer other research questions in the future. Only researchers who have the training and experience to do the research (also known as "qualified researchers") will be allowed to use the data and in no way can your data be linked back to you.

Who will be able to look at my data?
During research studies, the data we get must be accurate. Therefore, your study data may also be looked at by people from: the University of Alberta auditors and members of the Research Ethics Board.

By signing this consent form, you are saying it is ok for the principal investigator/staff to collect, use and disclose information from your study data as described above.

If you would like to see the study data collected about you, please ask a member of the research team. You will be able to look at the study data about you and you can ask for any mistakes to be corrected. We will have to wait until your participation in the study is complete to share your study data with you.

If you leave the study, we will not collect new information about you. Data already collected will be kept unless requested otherwise.

What if I have questions?
If you have any questions about the research now or later, or if you experience any adverse effects or think that you have suffered a research related injury please contact **Desi Fuhr (780-492-1121) or Michael Stickland (780-492-3995).**

If you have any questions regarding your rights as a research participant, you may contact the University of Alberta Research Ethics Office at reoffice@ualberta.ca. This office is independent of the study investigators.

The study investigators do not have any conflicts of interest to disclose. This study is funded by a federal grant called the Canadian Institutes of Health Research Project Grant. This means that the Institution and researchers are getting money from the granting agency/funder to cover the costs of doing this study. This funding does not involve any personal payments to the research team.

How do I indicate my agreement to be in this study?

By signing below, you understand:

- That you have read the above information and have had anything that you do not understand explained to you to your satisfaction
- That you will be taking part in a research study
- That you may freely leave the research study at any time
- That you do not waive your legal rights by being in the study
- That the legal and professional obligations of the investigators and involved institutions are not changed by your taking part in this study.

SIGNATURE OF STUDY PARTICIPANT

_____
Signature of Participant

_____ _____
Name of Participant Date

SIGNATURE OF PERSON OBTAINING CONSENT

_____
Signature of Person Obtaining Consent

_____ _____
Name of Person Obtaining Consent Date

SIGNATURE OF WITNESS

_____
Signature of Witness

_____ _____
Name of Witness Date

A signed copy of this consent form has been given to you to keep for your records and reference.