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PARTICIPANT CONSENT FORM (PARENT)

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 is my child being asked to take part in this research study?
Your child has been invited to participate because your child meets the eligibility criteria for one of the study groups. Depending on your child's product use, your child may be enrolled as:

- A control participant (your child does 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).

<u>This study will not involve any medications for experimental purposes.</u>

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

What is the reason for doing the study?
Electronic nicotine delivery systems (ENDS), including e-cigarettes, vapes, and vape pens, and cannabis smoking has 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 depend 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 4 visits ranging from 1 hour to ~4 hours per visit (~10 hours total). All visits will take place at the Clinical Physiology Laboratory located in the Clinical Sciences Building. Your child can take breaks as needed during the visits.

For all visits, we ask that your child 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 your child refrain from using ENDS for at least 6 hours prior to visits 2-4.

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 30 minutes
   Your child will complete questionnaires on an online survey system on a tablet. The questionnaires will ask about your child's use of electronic nicotine delivery systems (ENDS), e-cigarettes, and traditional cigarettes, as well as any respiratory symptoms your child 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
     Your child will be asked to fill out a detailed questionnaire about their electronic nicotine delivery systems (ENDS), e-cigarette and cigarette habits at different times during the study. This helps us track any changes in how your child uses these products over time. The questionnaire will cover things like:
       - What types of e-liquids your child uses, how strong they are, and how much your child uses them;
       - The flavors and brands of e-liquids your child prefers;

- What kind of devices your child uses and how often;
- How many times your child puffs on their e-cigarette each day
- How long your child has been using e-cigarettes.

We will also ask about your child's past and current habits with smoking regular cigarettes, using cannabis, drinking alcohol, and using illegal drugs at each time point. We will also ask your child if they 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 child's breathing issues affect their ability to do activities in their everyday life. Most questions are true or false (e.g. coughing hurts, true or false?).

- The American Thoracic Society Questionnaire (ATSQ): approximately 5 minutes
  This questionnaire will ask your child 8 questions on how their cough is affecting them.

- The Visual Analog Scale: approximately 5 minutes
  Your child will be asked to rate their breathing by drawing a line on a scale.

3. **Pulmonary Function Test:**
   Your child will undergo a Pulmonary Function Test, which involves breathing into a tube to assess how well their lungs work. The test will measure blockages in your child's 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 your child to breathe in and out forcefully into a small tube. This test measures the extent of obstruction in your child's 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 approximately less than one hour in total.

   - Oscillometry (approximately 30 minutes): This is a simple way for the doctor to measure your child's 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
   Your child will undergo a Cardiopulmonary Exercise Test (CPET) on a stationary bike. First, your child 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 your child will pedal until they can't continue.

5. **Activity Monitoring:** worn at home for 7 days
   Your child 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 if needed, or when removal is required for activities such as bathing and contact sports.

   A charger will be provided. After the 7-day period, you or your child will 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 your child will do several 6-second breath-holds at rest and during easy to very hard exercise on the same stationary bike used in their previous visit. The breath-holds let us look at your child's 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 child's heart rate, blood pressure, and oxygen saturation throughout. If your child experiences any discomfort, they 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, your child will do the same breath-holds as visit 2. Your child will do the breath-holds while lying on their back in the lower body pressure chamber. A lower body pressure chamber is a device that encloses their lower body (from their hips to their toes) and gently applies either positive pressure (LBPP) by pushing blood from the legs towards the chest, or negative pressure (LNBP) by pushing blood towards the legs. Your child's lower body will be sealed within the chamber via a compression skirt to prevent any air leakage from the insides of the chamber. The pressure chamber allows us to safely study how the blood vessels in your child's lungs respond to changes in blood flow. At each pressure level, your child will do 2 breath-holds.

We will also measure your child's heart rate, blood pressure, vein pressure, and oxygen saturation throughout. A fingertip prick blood sample will be collected twice during the visit, once at the beginning and another time towards the end of the test. Your child 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, your child 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 laying down in the lower body pressure chamber, your child 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 child's

heart, similar to the changes that occur naturally when they stand up or lie with their feet above their head. The pressure levels used in this test are designed to produce mild, temporary changes in blood flow and blood pressure. Your child may experience sensations such as lightheadedness, dizziness, or discomfort during the pressure changes. The research team will monitor your child throughout the test, and your child may take a break or stop the test at any time if they 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, your child 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 child's chest to take pictures of their heart. The ultrasound uses sound waves to create images of your child's heart and is painless. These images help us see how your child's heart pumps and responds to exercise and changes in blood movement. Your child will have the opportunity to rest between stages.

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: Your child may feel uncomfortable answering some of the questions. Your child does not have to answer any question that they 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 child's race or ethnic origin is voluntary.

Pulmonary Function Tests: Lung function tests may make your child feel short of breath or dizzy. We encourage your child to inform the technician or study coordinator if they feel this way during the test. If your child experiences any discomfort, they 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 your child to take breaks or stop the procedure at any time.

Cardio-Pulmonary Exercise Test (CPET): During the CPET, your child will perform exercise that gradually becomes more difficult until your child reaches their maximum effort or can no longer continue. This is a maximal exercise test designed to assess how your child's 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 your child has 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 your child has conditions like COPD or asthma, CPET might worsen their 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 your child already has muscle or joint problems or is 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, your child 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 your child to continue. Your child may stop the test at any time if they feel unable or unwilling to continue. Should your child experience any symptoms during or following their test, a trained researcher will stay with your child until they 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 and procedures are in place to ensure your child's safety.

If your child has any questions or experiences any unexpected symptoms after your child's study visit, please contact the research team using the contact information provided at the beginning of this consent form. If your child's 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.

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

Finger Prick Blood Sample: Your child may feel minor discomfort as their finger is pricked.

Ultrasound Imaging: There are no known risks to ultrasound imaging of the heart or blood vessels. However, your child may feel some discomfort during the heart imaging as the ultrasound probe will be pressed against their chest. If an abnormal finding is discovered, we will inform your child of this.

Pregnancy: If your child is a woman of childbearing potential not using contraception, your child will be asked to have a negative urine pregnancy test before starting the study. We will provide a test for your child. 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 your child practices abstinence it is important to use another method of birth control if they 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 child's information used in this study will be handled and stored securely and nothing that identifies your child 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 your child. No information from this study will become part of your child's health record. However, if an abnormality is detected and further follow-up is required, then this information may become part of your child's health record.

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

What are the benefits to my child?
There will be no direct benefit to your child 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 my child is injured because of this research?
In the case of research-related side effects or injury, your child will be referred for appropriate medical care.

What are the rights of participants in a research study?
You and your child will be told, in a timely manner, about new information that may be relevant to your child's willingness to stay in this study. Your child's rights to privacy are

legally protected by federal and provincial laws that require safeguards to ensure that their privacy is respected.

By signing this form, your child does not give up any of their 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.

Does my child have to take part in the study?
Being in this study is you and your child's choice. If your child decides to be in the study, they can change their mind and stop being in the study at any time, and it will in no way affect the care or treatment that your child is entitled to.

What will it cost my child to participate?
Participating in this study will not cost your child anything. Your child will be reimbursed for parking or transit costs associated with each study visit.

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

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

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

What data will we be collecting?
During this study we will be collecting data about your child. Examples of the types of data we may collect include your child's 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 your child 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 child's 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 child's name to anyone unless required by law.

How will the study data be used?
Your child's study data will be coded (with a number) so that it no longer contains your child's name or anything else that could identify them. Only investigators will be able to

link your child's coded study data to your child. The risk to your child's privacy, then, should be very small.

When the study is done, the investigators may place your child's 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 child's data be linked back to them.

Who will be able to look at my data?
During research studies, the data we get must be accurate. Therefore, your child's 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 and your child are saying it is ok for the principal investigator/staff to collect, use and disclose information from your child's study data as described above.

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

If your child leaves the study, we will not collect new information about them. Data already collected will be kept unless requested otherwise.

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

If you or your child have any questions regarding their rights as a research participant, you or your child 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 your child will be taking part in a research study
- That your child may freely leave the research study at any time
- That your child does not waive their legal rights by being in the study
- That the legal and professional obligations of the investigators and involved institutions are not changed by your child's taking part in this study.

I agree to allow my child _____ to take part in this study.

(CHILD's NAME)

SIGNATURE OF PARENT OR LEGAL GUARDIAN

I have the legal authority to give this consent.

Signature of Parent or Legal Guardian _____

(Printed Name) _____

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 your child to keep for their records and reference.