Document Coversheet

Study Title: Effects of Tobacco Flavoring and Liquid Composition on Vaping Topography

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ROSWELL PARK CANCER INSTITUTE

Title: Effects of Tobacco Flavoring and Liquid Composition on Vaping Topography

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Roswell Park Study Number: I-3234822

Consent Form Given to Participant Taking Part in a Research Study

KEY INFORMATION ABOUT THIS RESEARCH STUDY

This is a research study being done by doctors at Roswell Park Comprehensive Cancer Center (the study sponsor). Research studies include only those people who choose to take part. Your participation is voluntary. Please take your time to make your decision. Discuss it with your family and with people who are important to you.

We are asking you to take part in this study because you are a healthy volunteer who responded to the recruitment campaign and meets the eligibility requirements of the study.

This study examines whether vape flavors or synthetic nicotine (nicotine made in a lab, not from tobacco leaves) are related to harmful effects on your health from vaping. This includes whether flavors or synthetic nicotine affect puffing patterns, appeal, risk beliefs, or perceived harshness or irritation.

Study Purpose:

The first main goal of this study is to examine the influence of tobacco flavoring on vaping topography (the way a person puffs on a vape). The second goal is to examine the influence of synthetic nicotine (made in a lab) vs. tobacco derived nicotine (from tobacco leaves) on vaping topography: this includes examining differences in sensory effects (such as harshness, irritation, taste strength) and subjective (how you personally feel about) effects (such as liking, enjoyment) by tobacco flavoring composition and by synthetic vs tobacco derived nicotine.

Study Duration and Number of Participants: Overall, this study will continue until the needed number of participants are enrolled. It is expected this will take about 18 months. This study will include about 72 participants in the Greater Buffalo and Rochester Regions. We expect to enroll about 36 participants from Roswell Park over 18 months.

Your participation in this study will be for 7 laboratory visits, approximately 1½ hours each, completed over about a 3 month period. Each visit will be scheduled a minimum of 24 hours and a maximum of 1 week apart.

Research Tests and Procedures: If you take part in this study, you will have the following tests as part of your participation.

- You will provide saliva samples before and after using the study products (collected three times during each session).
- Females of child-bearing age will be asked to provide a urine sample and be tested for pregnancy during the first session, prior to using the study product.
- You will be asked to complete the study survey questionnaires (once at the beginning of each session and at two additional timepoint during the session) – these questionnaires are designed to look at different aspects of upper airway sensation and subjective effects, preferences (e.g., food), mood, and decision making.
- You will use equipment designed to measure your vaping patterns during vaping. This device is attached to the vaping product mouthpiece and measures airflow.
- You will provide an oral rinse sample using mouthwash (Roswell Park only; first session only – this is optional)

We would like to store leftover samples of your saliva and oral rinse, to be used for future research. The Optional Research section at the end of the consent form provides additional details. Choosing not to provide additional samples or leftover samples for additional research will in no way affect your being able to participate in the study.

Section 1 of this document provides additional information on the tests and procedures involved with this study.

Study Costs:

There are no costs to you associated with this study.

Side Effects and Risks: While you take part in this study, you may be at risk for:

- Nicotine withdrawal: Many individuals who stop nicotine use exhibit a pattern of symptoms related to withdrawal, which may include: sadness and anxiety, irritability, anger, difficulty concentrating, appetite change and weight gain, insomnia, and decreased heart rate. Because you will be asked to refrain from nicotine use before the session, it is likely that you will experience some of these symptoms.
- Nicotine overdose: Some people who use nicotine products may experience symptoms of nicotine overdose such as nausea, sleep disturbance, headache, and vomiting; however, these symptoms are usually mild and temporary.
- Respiratory irritation: Some people who vape may experience irritation of the linings of their airways, but this may not be likely as you are already a vaper. If a participant demonstrates chronic or acute breathing problems, you may be withdrawn from the study or procedures may be postponed.
- Inconvenience: It is possible that participants will experience inconvenience due to multiple study visits required.
- Emotional distress: Participants may experience psychological discomfort during assessments when discussing feelings and attitudes about smoking and using nicotine products, or from learning about the risks of vaping. However, all participants will be current smokers and we do not expect this type of reaction to be likely. Study personnel

will be alerted to expect this from a small number of participants and will be trained to make referrals for mental health services as needed. Personnel will be trained to query for adverse emotional reactions during assessments and will be trained to deal with such reactions and to provide additional referrals if needed. In addition, if assessments indicate psychiatric concerns, referrals to appropriate psychological services will be provided.

- Reproductive Risks: Women will be advised to notify the study staff if they become or intend to become pregnant during the study period. Because nicotine and ENDS vapor safety for an unborn baby is unknown, participants will be told that they should not become pregnant while on this study nor should they nurse a baby. If a woman is pregnant or breastfeeding, she may not participate in this study, and if she becomes pregnant during the study, she will be removed from the study.
    - These e-liquids have not been studied in pregnant women, and there may be potential unknown risks with exposure. Women should not use vaping products, including e-liquids, during pregnancy and should avoid pregnancy during the study.

You should discuss these risks with your doctor/study investigator.

The nicotine present in the products is considered a stimulant (affects energy) as well as an anxiolytic (affects symptoms of anxiety such as feelings of fear, dread, uneasiness and muscle tightness, that may occur as a reaction to stress). Participants can choose, as an alternative, to not enroll in this study.

Overall, there is minimal risk for serious adverse reactions as a consequence of enrolling in this study.

The risks for this study are anticipated to be minimal.

Section 4 of this document provides more detailed information on possible side effects and risks.

Potential Benefits:

You understand there is no guarantee that being on the study will help you. Future participants may be helped from the results and information gained from this study.

Other Options:

It is your decision to join. There are no penalties for not taking part in this study.

The type of study, the risks, benefits, discomforts, and other important information about this study are discussed below.

ADDITIONAL INFORMATION ABOUT THIS RESEARCH STUDY

It is important that you read and understand the following facts that apply to anyone that takes part in our studies:

a) This study is considered research. It is investigational.
b) Taking part in the study is voluntary.
c) You may withdraw from the study at any time without penalty, loss of any benefits or access to care at Roswell Park to which you are otherwise entitled.
d) Personal benefit may not result from taking part in the study, but knowledge may be gained that will benefit others.

e) If we become aware of important new information that might influence your willingness to participate in the study we will inform you.

f) If you decide to stop being in the study, you should talk with your doctor first about this decision so you are informed whether stopping study participation may have any effects on your health.

1. If I take part in this study, what tests and procedures will I have done?

You are to abstain from vaping for at least 30 minutes prior to each session.

At the beginning of the first study session, you will complete a taste test to ensure your sense of taste is intact. You will complete phenylthiocarbamide (PTC), 6-n-propylthiouracil (PROP), and sodium benzoate tasting, using manufactured, pre calibrated strips: These compounds are present in various naturally occurring foods and are related to one's ability to taste if something is sweet, salty or bitter. You will be directed to place the taste test strips on your tongue and determine if you taste a flavor. Women of child-bearing potential will also be asked to provide a urine sample and must test negative prior to receiving any study-related products/procedures. Following the taste test at the beginning of the first session, at each laboratory session, you will be completing questionnaires, giving saliva samples, and completing a vaping task.

Each vaping task will require you to vape as directed (4 second puffs on the device every 60 seconds until a total of 8 puffs is complete) and ad lib (i.e., as much or as often as you like) for 15 minutes using a SmokTech® NORD2 or equivalent device. The order that you vape as directed or ad-libbed will be randomized per session.

Saliva Sample Collection

Step 1. Open foil pouch and remove the saliva collection tube

Step 2. Place ribbed-end of the tube securely into a pre-labeled collection vial

Step 3. Allow saliva to pool in mouth. Then, with head tilted forward, gently force saliva through the tube into the vial. Fill to required volume.

Step 4. Remove and discard tube. Attach cap to collection vial and tighten.

Session 1:

You will first give a saliva sample and complete a set of pre-task questionnaires. You will then vape your own brand either directed or ad lib randomized per order. Then, you will give a saliva sample via a swish and spit method (spitting into a tube) and answer post task questionnaires. The entire task will be repeated beginning with the vaping task either directed or ad lib per the randomization. This session will be approximately 90 minutes long.

Sessions 2 – 5:

You will first give a saliva sample complete a set of pre-task questionnaires. You will then vape one of 4 vape tobacco flavors (3 tobacco and 1 unflavored) randomized per session either directed or ad lib randomized per order. Then, you will give a saliva sample via a swish and spit method (spitting into a tube) and answer post task questionnaires. The entire task will be repeated beginning with the vaping task either directed or ad lib per the randomization. These sessions will be approximately 90 minutes long.

Sessions 6 & 7:

You will first give a saliva sample and complete a set of pre-task questionnaires. You will then vape one of 2 nicotine types (synthetic nicotine or tobacco derived nicotine) randomized per session either directed or ad lib randomized per order. Then, you will give a saliva sample via a swish and spit method (spitting into a tube) and answer post task questionnaires. The entire task will be repeated beginning with the vaping task either directed or ad lib per the randomization. These sessions will be approximately 90 minutes long.

General Study Timeline:

-15 min	PROP, PTC, Sodium Benzoate, urine sample (women of child-bearing potential) (1st session only) Roswell Park participants ONLY: Saliva
-10 min	Pre: Questionnaires
0 min	Begin *bout 1*
15 min	End *bout 1* / Collect Product
20 min	Post: Saliva
20 min	Post: Questionnaires
45 min	Begin *bout 2*
60 min	End *bout 2* / Collect Product
65 min	Post: Saliva
65 min	Post: Questionnaires

2. Will I be informed of research results?

All analyses will be completed as a group. Though the goal is to publish the overall results in a scientific journal made available to the public, no individual's results or information will be shared either with the participant or public.

3. Why would I be taken off the study early?

You may be taken off the study for any of the following reasons:

- You do not follow the study schedule or requirements
- New information becomes known to us that would influence your decision to remain on the study

- Your medical condition changes
- You experience unacceptable side effects
- The study doctor or the sponsor of the study may decide to stop or change the study.

4. What risks and discomforts are involved?

The procedures used in this study may cause all, some, or none of the side effects listed. There may be other side effects of the procedures that we do not know of yet. The risks and side effects for the study procedures, e-liquids, and questionnaire are listed below.

Taste Tests: There is no to minimal risk for placing a piece of paper on your tongue to detect a flavor.

E-liquids and Vaping Devices: The liquids and devices used in this study are commercially available products purchased from local retail vendors. The long-term risks of vaping are currently unknown.

Survey: The study will only involve your provision of responses to questions. The chance of risk or discomfort is 'none to minimal'. In the unlikely event of distress caused by participation in the study, Dr. O'Connor from the Department of Health Behavior will be available to identify psychological resources for you. If you are affected, Dr. O'Connor will be available to consult with your primary care physician regarding care and referral for you.

Saliva Collection: There is no to minimal risk for spitting into a tube.

Oral Rinse collection: There is no to minimal risk for using a commercial mouthwash and spitting into a vial.

It is very important that you notify your doctor/study investigator right away about any side effects, problems, or unusual experiences you may have while on this study. This will decrease the chance that the side effects continue or become worse. Sometimes there are other resources that we can provide to you to make you more comfortable. If severe side effects do develop, you and your doctor/study investigator may decide it is in your best interest to stop taking part in the study.

5. Reproductive risks:

These e-liquids have not been studied in pregnant women, and there may be potential unknown risks with exposure. Women should not use vaping products, including e-liquids, during pregnancy and should avoid pregnancy during the study.

This study may involve risks to you or your unborn child that are not known at this time therefore, you should not become pregnant or father a baby while you are participating in this study. Also, you should not nurse your baby while on this study. Women of childbearing potential will be required to take a pregnancy test before being allowed to take part in this study. You may also be asked to take pregnancy tests during the study. The pregnancy test must be negative before you enter this study.

Women of childbearing potential will be asked to practice an effective method of birth control while on this study. This includes, but is not limited to, oral birth control pills, an IUD, condoms with spermicide, or abstinence. To the best of your knowledge, you are not pregnant and do not plan to become pregnant while taking part in this study. Should you become pregnant during this study, you need to immediately tell your study doctor and obstetrician. If you wish you may request

a referral for counseling or ask about counseling (such as genetic counselor, social worker, or psychologist) to discuss this further.

6. What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Follow directions of the study personnel
- Abstain from tobacco/nicotine use for at least 30 minutes prior to each session
- Provide honest answers to all questionnaires
- Be respectful to other participants and study personnel

7. What happens if I am injured as a result of this study?

If you believe you have been injured as a direct result of your participation in this research study, notify the Roswell Park Patient Advocate at (716) 845-1365 or the Study Doctor at (716) 845-4517.

Medical diagnosis and treatment for the injury will be offered, and a determination will be made regarding appropriate billing for the diagnosis and treatment of the injury. A financial counselor can be reached at 716-845-3161 to provide an explanation of coverage and to answer questions you may have regarding study related billing.

You do not give up any legal rights by signing this form. You are not prevented from seeking to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research.

8. Will I be paid for joining this study?

You will receive the following payment for participating in this study:

Participants will be compensated with an Amazon Gift Card Code sent to their provided email. A gift card code will be sent within 24 hours of the session completion. Funds are immediately available when added to their Amazon account and participants can check their balance as desired. This system will allow frequent, immediately available payments.

Funds will be added to card upon successful completion of each session as follows:

Session 1: $25
Sessions 2 - 5: $30
Sessions 6 & 7: $50
Completion Bonus: $50

If all sessions are successfully completed, you will earn a total of $295.

It is possible that this research project may result in developing treatments, devices, new drugs, or procedures that could be used for commercial profit by the sponsor or other entities. If this happens, you understand that you will not receive any financial payment or share in any commercial profit for the use of your information and biospecimens (such as blood or tissue samples) collected as part of this research.

9. Where can I find more information?

You may call the NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

For accurate cancer information including Physician Data Query (PDQ), visit https://www.cancer.gov.

10. Who do I contact with questions?

You are free to ask questions at any time about this study and to ask for more information from the doctor identified on this document. If you have any questions, concerns or complaints about this study, you should contact the study doctor identified on the first page of this document. In case of an emergency after regular hospital hours, you should telephone (716) 845-2300 and ask for the medical doctor on call.

If you have questions about your rights as a research subject or you feel you have been injured as a result of your participation in this research study, you can call the Roswell Park Patient Advocate (Support) Office at (716) 845-1365. You should also feel free to contact the Patient Advocate Office at any time while considering participation, during participation or once your participation is complete. This office is unaffiliated with any specific research study. They can help you obtain additional information regarding your research participation and your rights as a research subject or how to proceed should you feel you have been injured as a result of your participation. They are available to discuss any problems, concerns, questions or input you may have.

11. Conflict of Interest Statement

The National Institutes of Health (NIH) pays for the conduct of this study, including part of Dr. O'Connor's salary.

- Any questions regarding financial conflict issues can be directed to your doctor or to Donald Handley, Executive Director, Office of Research Subject Protection, who can be reached at 845-3455.
- This disclosure is made so that you can decide if this relationship will affect your willingness to participate in this study.

What about confidentiality?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information collected in this study may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect the study records and your information. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The study sponsor supporting the study.
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.

- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

Information that does or can identify you may be removed from your information or biospecimens (such as saliva) so that it may be used or disclosed for other purposes, including use for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

To ensure data security and confidentiality, all assessments will be administered by trained research study staff. Data collected and stored via REDCap (Research Electronic Data Capture). REDCap is a secure web-based application that supports data collection and management for research studies. All participant records and data will be held in the Health Behavior Department at Roswell Park Comprehensive Cancer Center. Access to the data by all necessary research personnel will be through a password protected network computer.

Certificate of Confidentiality

As an additional measure to protect your privacy, a Certificate of Confidentiality has been issued from the United States Government, National Institutes of Health, for this study. With this Certificate, the investigators and institutions involved in this study 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 proceeding. We will use this Certificate to resist any demands for information that would identify you, with the following exceptions:

- The Certificate cannot be used to resist a request for your information from the United States Government when the information is to be used for auditing or evaluation of federally funded projects or for information that must be disclosed to meet the requirements of the Food and Drug Administration (FDA).
- State law requires we report cases of diseases that spread easily, or abusive behavior (toward a child, a partner, or an elderly person), and people who say they are going to hurt themselves or someone else.
- The Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or involvement in this research. Also, if you have given written consent to an insurer, employer, or other person to receive research information, then we may not use the Certificate to withhold the information.

OPTIONAL RESEARCH

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The research from these studies may help other people with cancer or other diseases in the future. You can still take part in the main study even if you say "no" to this optional research.

If you choose to take part, your samples will be de-identified from personal information and stored in Dr. Goniewicz's lab as noted above and extra saliva samples will be collected. These samples will also be de-identified and stored in Dr. Goniewicz's lab. These samples will be collected when the study saliva sample is taken.

We will not give researchers information that could directly identify you. We will take many steps to protect the privacy of people who take part. We will remove your name and any other

information that could directly identify you from your samples and information. We will replace the direct identifiers with a code number and only certain study staff will have access to the key that will link the code number to your identity. By protecting your identity in this manner, researchers who study your samples and information will not know who you are. There is a risk that someone could get access to the data we have stored about you. It is also possible that the information from your genome, when combined with information from other public sources could be used to identify you. We believe the chance of this happening is very small but we cannot make guarantees. Your privacy and the confidentiality of your information are very important to us and we will make every effort to protect them.

It is not possible for us to know now what tests will be discovered in the future. We cannot give you a list of all the possible ways the sample will be used. We are asking that you give your permission for us to store and do research on the sample without contacting you again in the future. It is possible that future research projects may result in developing treatments, devices, new drugs, or procedures that could be used for commercial profit. If this happens, you understand that you will not receive any financial payment or share in any commercial profit for the use of your biospecimens (such as blood or tissue samples) that had been stored for future research.

If you give permission for the sample now and change your mind later, you will need to write to the doctor listed on the first page of this form and let him/her know that you changed your mind. If we have not already used the sample, it will be destroyed and not used. If you have any questions, please ask your doctor.

My leftover saliva can be used in research to learn about, prevent, treat, or cure cancer.

PLEASE CHECK ONE BOX

YES ☐ **NO** ☐

My oral rinse sample can be taken and used in research to learn about, prevent, treat, or cure cancer.

PLEASE CHECK ONE BOX

YES ☐ **NO** ☐

I agree that someone may contact me in the future to ask me to take part in more research.

PLEASE CHECK ONE BOX

YES ☐ **NO** ☐

Statement of Investigator/Person Conducting the Informed Consent Discussion:

I certify that the nature and purpose, the potential benefits and possible risks associated with participation in this research study have been explained and that any questions about this information have been answered. A signed copy of this consent will be given to the participant.

SIGNATURE_____ **DATE**_____ **TIME**_____

PRINTED NAME _____

Participant's Statement of Consent:

By signing below, you agree that:

- You have been told of the reasons for this study.
- You have had the study explained to you.
- You have had all of your questions answered, including those about areas you did not understand, to your satisfaction.
- You have carefully read this consent form and will receive a copy of this form.
- You do **not** waive any **legal** rights you have under federal or state laws and regulations.
- You willingly give your consent to voluntarily join in this research study.

Participant:

SIGNATURE_____ **DATE**_____ **TIME**_____

PRINTED NAME _____

Witness Signature is needed in the following circumstances – check below:

☐ Not Applicable
☐ The person consenting cannot write – mark must be made as appropriate.
☐ The person consenting cannot read - consent has been read to him/her.
☐ The person consenting cannot understand English and the consent has been verbally interpreted.

(The witness should be fluent in both English and the language of the person consenting.)

Witness Statement:

The person consenting has signed this document in my presence.

SIGNATURE_____**DATE**_____ **TIME**_____

PRINTED NAME _____

RELATIONSHIP TO PARTICIPANT_____