RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM

STUDY TITLE: The Abuse Liability of a Novel Heated Tobacco Product (IQOS) and Its Feasibility as a Menthol Cigarette Substitute (HTP-FLAVORS)

VCU INVESTIGATOR: Dr. Andrew Barnes, Associate Professor of Health Behavior and Policy

SPONSOR: National Institutes of Health/Food and Drug Administration (FDA)

ABOUT THIS CONSENT FORM

You are being invited to participate in a research study lead by VCU's Dr. Andrew Barnes. **It is important that you carefully think about if being in this study is right for you and your situation.**

This consent form is meant to assist you in thinking about whether or not you want to be in this study. **Please ask the study staff to explain any information in this document that is not clear to you.** We will email you an unsigned copy of this consent form to think about and discuss with family or friends before making your decision.

Your participation is voluntary. You may decide to not participate in this study. If you do participate, you may withdraw from the study at any time. Your decision not to take part or to withdraw will involve no penalty or loss of benefits to which you are otherwise entitled.

AN OVERVIEW OF THE STUDY AND KEY INFORMATION

This study aims to understand how the flavors ("Tobacco" and "Menthol") for a *heated tobacco product* called "IQOS" impact tobacco use, nicotine exposure, and the chance someone might use these products. IQOS was authorized by the U.S. FDA as a product that exposes smokers to less harmful chemicals than cigarettes. This study focuses on menthol smokers because they have been shown to have a harder time quitting than non-menthol smokers. Additionally, FDA is considering banning menthol in cigarettes and heated tobacco products. This study will help us to understand heated tobacco product flavors and their potential to reduce harm among smokers.

In this study, you will be asked to do the following things:

1. **To begin**, we will ask you to complete a brief online "pre-screener" where we will ask about your background, medical history, and tobacco use.
2. **If your responses indicated that you are potentially eligible for the study**, we will contact you to schedule an in-person screening session at VCU's Center for the Study of Tobacco Products (CSTP). At this session we will confirm your identity, review study procedures, and discuss your consent to participate.

   You may skip any survey questions administered (at any point in the study) except for those required to determine your eligibility.

3. **If you consent to participate in the study**, you will complete a survey during the in-person screening session. If you are eligible, we will ask that you return to the CSTP on a Monday (within 2 weeks) to begin the study. If you are not eligible, you will be paid for screening ($25) but removed from the study. During this session, we will ask for a urine sample to test for pregnancy (pregnant individuals are not

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eligible) and the presence of cotinine to confirm your status as a smoker. We will also collect a breath sample to test for carbon monoxide, by having you breathe through a specialized instrument for 10 seconds. You will also have an opportunity to take up to 4 test puffs of the study product in the tobacco flavor. This session may last about 1 hour.

4. **If you complete the screening session**, the first full-week of the study is called the "baseline week." You will come to the CSTP on both Monday and Friday of this week for about 2 hours. We ask that you refrain from using nicotine containing products for the 8 hours before t session. However, not refraining from using nicotine containing products will not stop you from being able to complete a session. During the course of these sessions, you will use your own brand menthol cigarettes (provided for free).

   During these lab sessions you will complete a series of activities to measure your tobacco use. First, you will answer questions about how you feel in that moment. Next, you will take 10 puffs of your cigarette during which we will monitor the length of the puffs you take and collect 2 blood samples. Last, you will complete an "experimental tobacco marketplace" where you will tell us how many cigarettes and other tobacco products you would buy if they cost varying amounts of money.

   You will report the number of cigarettes and other tobacco products you use while at home. These surveys will be sent using text message or email (your preference). Messages will be sent every morning at 8 AM and ask about your tobacco use over the prior day.

5. **If you successfully complete the baseline week lab sessions**, you will be randomized to receive one of two flavors of IQOS: menthol or tobacco. This means your condition assignment (i.e., which products you will receive) will be determined purely by chance, like flipping a coin. You will have an equal chance to be in a condition where you will receive the heated tobacco product in:

Tobacco flavor

OR

Menthol flavor

6. **Beginning on the Monday of the intervention week**, this will mark the start of the "intervention week". This week follows the same procedure as the baseline week but instead of using your own brand menthol cigarettes, we will ask you to replace some or all of your normal cigarette use with IQOS products. We will give you these products to take home. We will continue to send you daily surveys. We will ask that your return all IQOS products on the following Friday .

Brief "pre-screener"	In-Person Screening Session and Informed Consent	Week 1 (Baseline week; Use your own brand menthol cigarettes)	Week 2 (Intervention week; Use your randomly assigned IQOS products)

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• Answer demographic and tobacco use questions • Schedule an in-person screening session and review an unsigned copy of this consent form	• Review informed consent document and provide consent • Complete screening survey and provide urine and breath samples • Complete baseline survey • Confirm eligibility • Take 4 tests puffs of the study product	• Use your own brand menthol cigarettes as you normally would • Respond to daily surveys • Participate in clinical lab sessions on Monday and Friday (2 blood draws, 10-puffs of your own brand menthol cigarette, hypothetical purchasing task, answering survey questions about subjective feelings and tobacco use)	• Attempt to replace some or all of your normal menthol cigarette use with IQOS (menthol OR tobacco flavor) • Respond to daily surveys • Participate in clinical lab sessions on Monday and Friday (2 blood draws, 10-puffs of IQOS, hypothetical purchasing task, answering survey questions about subjective feelings and tobacco use)

WHAT WILL HAPPEN IF I PARTICIPATE IN THE STUDY?

Your participation in this study will last about 3 weeks. The brief online screener and in-person screening session should take about 1 hour total. Each clinical laboratory session during the baseline and intervention weeks will take about 2 hours. The daily surveys will take <3 minutes per day over two weeks. Total study involvement is expected to be about 10 hours. About 50 individuals will participate in this study. Below, we provide a brief description of all study measures:

1. **Blood Plasma Nicotine/Menthol Levels and Puff Topography (Clinical Lab Sessions ONLY):** At the start of the 4 clinical lab sessions, our research nurse will prepare your arm to obtain a blood sample – either via venipuncture (“a stick”) or (if necessary) by placing a catheter. Once your arm has been prepared, a 7 mL (about 1.5 tsp) sample of blood will be taken by a registered nurse. You will then complete a “puffing bout” with that session’s designated product (own brand menthol cigarettes [baseline week] or IQOS [intervention week]), in which research staff will direct you to take 10 puffs of the product with a 30-second break between puffs. Your tobacco product will be connected to a machine that measures how long you are puffing and the volume of air you inhale. After the puffing bout, another 7 mL blood sample will be taken (14 mL/session).

2. **Subjective Effects Questionnaires (Clinical Lab Sessions ONLY)**: Immediately before and after the puffing bout described above, you will complete a short set of questions about how you are feeling in that moment regarding cigarette cravings, mood, and nicotine withdrawal symptoms.

3. **Experimental Tobacco Marketplace (Clinical Lab Sessions ONLY):** After the subjective effects questions, you will have a 15-minute rest period. You will then complete the “Experimental Tobacco Marketplace.” In this task, you will be provided with a (hypothetical) budget and asked how you would spend that money across multiple tobacco products at various prices. You will not receive any of the products you select for purchase.

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4. **Daily Tobacco Use Questionnaires (Every day, at home):** Beginning on Monday of the baseline week and continuing until Sunday of the intervention week, you will receive a text- or email-based invitation to complete a short survey. The survey will ask about the type and amount of tobacco products you used over the prior day. Surveys will be sent at 8 AM each day.

WHAT ALTERNATIVES ARE AVAILABLE?

This is not a therapeutic study. You have the alternative not to participate.

WHAT RISKS AND DISCOMFORTS COULD I EXPERIENCE FROM BEING IN THE STUDY?

There are both risks and benefits of participating in research studies.

Most Common Risks and Discomforts

Physical Risks:

1. Frustration - You may experience mild frustration while completing some of the study-related questionnaires.
2. Breath sampling for carbon monoxide - You may find giving breath samples uncomfortable but using a special collection device should reduce this risk. Moreover, it is possible that holding one's breath and breathing out for 10 seconds could cause some temporary lightheadedness and discomfort. However, such effects should resolve spontaneously for participants that meet inclusion standards for physical health.
3. Nicotine-related side effects - You may experience side effects from products that contain nicotine such as acute increases in heart rate and blood pressure, sweating, lightheadedness, dizziness, nausea, and nervousness. These side effects are unlikely in individuals who use cigarettes regularly.
4. Heated tobacco product side effects - The use of heated tobacco products may include other side effects/risks such as cough, headache, and syncope (fainting). Available data indicates side effects from these products are similar to other tobacco exposures.
5. Nicotine withdrawal symptoms – Some participants may experience nicotine withdrawal symptoms when they reduce their own brand cigarette consumption. Common withdrawal symptoms are irritability, anxiety, depressed mood, increased appetite, fatigue, or difficulty concentrating. These effects may also be experienced by individuals when adhering to the 8-hour abstinence period preceding each clinical lab session. These effects are seldom clinically-significant but will be monitored by the researchers.
6. New pregnancy or want to become pregnant – Nicotine, either from cigarettes or heated tobacco products, is known to be harmful to the developing human fetus. Women who are pregnant or are nursing a child may not participate in this research study. You must agree to take reasonable and necessary precautions against becoming pregnant during the period of the investigation. The investigator will discuss appropriate precautions with you. If at any point during the research you believe there is any possibility that you may be pregnant, you must notify the research assistant or research nurse immediately.
7. The researchers will let you know about any significant new findings (such as additional risks or discomforts) that may make you change your mind about participating in the study.
8. Blood draws - there is possible risk of bruising, infection, and discomfort resulting from the two blood draws that will be conducted during each clinical session. These are routine medical procedures and we attempt to mitigate these risks by having trained personnel (research nurse)

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perform all blood draws using aseptic techniques. Such adverse effects of blood draws are typically minor and/or uncommon when performed with proper technique by a trained professional. Our medical monitor is available to evaluate and provide necessary referrals in the event that any adverse complication arises from these blood draws.

Non-physical Risks
1. Privacy - Participation in research might involve some loss of privacy. There is a small risk that someone outside the study could see and misuse information about you.
2. Sensitive questions - The study questionnaires ask personal questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable.

Benefits to You & Others
1. You will derive no personal benefits from this study. Your participation will help us to better understand the effects of flavors in heated tobacco products.
2. In general, we will not give you any of your individual results from this study.

WILL I BE PAID TO PARTICIPATE IN THE STUDY?

Payments from this study will be paid out in cash in US Dollars.

Following the brief online "pre-screener" and obtaining of informed consent, you will be asked to complete the screening session for $25. If your responses indicate you are eligible, you will be asked to participate in 4 clinical lab sessions over a 2 week period (2 sessions/week). Lab sessions will take place on Monday ($50/session) and Friday ($100/session) of each week. Additionally, you will be asked to complete daily surveys (<3 min) reporting your tobacco use from the previous day ($2/day for 2 weeks = $28 total). The total possible payment if you complete all study activities (in-person screening, 4 clinical lab sessions, 14 daily surveys) is $353. You will be paid all money due for study activities completed to-date at 5 times: after the in-person screening session and after the 4 in-person clinical lab sessions. We can also reimburse you up to $12 per visit for parking, if needed.

If you decide to stop participating, you are entitled to compensation for all study activities completed to that point. This partial compensation can either be paid out in cash (USD) by coming to the CSTP or by requesting a giftcard be sent to your email account (Amazon giftcards ONLY).

How you are paid for completing each activity in this study

	In-Person Screening Session	Monday Lab Sessions (x2)	Friday Lab Sessions (x2)	Daily Surveys (x14)
Amount	$25 for completing the in-person screening session.	$50 during both Weeks 1 and 2	$100 during both Weeks 1 and 2	$2 per day during Weeks 1 and 2
Total Possible: $353	$25	$100	$200	$28

Total payments within one calendar year that exceed $600 will require the University to annually report these payments to the IRS and you. This may require you to claim the

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compensation you receive for participation in this study as taxable income. VCU is required by federal law to collect your social security number. Your social security number will be kept confidential and will only be used to process payment.

WHAT HAPPENS IF I AM INJURED OR BECOME SICK BECAUSE I TOOK PART IN THE STUDY?

If you are injured by, or become ill, from participating in this study, please contact the main study site (804-827-3562) and/or your study doctor (Dr. Thokozeni Lipato; thokozeni.lipato@vcuhealth.org) immediately. Medical treatment is available at the Virginia Commonwealth University Health System (VCU Health System). Your study doctor will arrange for short-term emergency care at the VCU Health System or for a referral if it is needed.

Fees for such treatment may be billed to you or to appropriate third party insurance. Your health insurance company may or may not pay for treatment of injuries or illness as a result of your participation in this study. To help avoid research-related injury or illness, it is very important to follow all study directions.

CAN I STOP BEING IN THE STUDY?

You can stop being in this research study at any time. Leaving the study will not affect your medical care, employment status, or academic standing at VCU or VCU Health. Tell the study staff if you are thinking about stopping or decide to stop.

If you leave the study before the final regularly scheduled assessment, you will be able to keep any money that you have earned in the study up to that point.

Your participation in this study may be stopped at any time by the investigator without your consent. The reasons might include:

- the investigator thinks it necessary for your health or safety
- you are found to not be eligible for the study
- the sponsor has stopped the study
- you have not followed study instructions
- administrative reasons require your withdrawal

HOW WILL INFORMATION ABOUT ME BE PROTECTED?

VCU and the VCU Health System have established secure research databases and computer systems to store information and to help with monitoring and oversight of research. Your information may be kept in these databases but are only accessible to individuals working on this study or authorized individuals who have access for specific research related tasks.

Identifiable information in these databases are not released outside VCU unless stated in this consent or required by law. Although results of this research may be presented at meetings or in publications, identifiable personal information about participants will not be disclosed. While you are participating in this study, only IRB-approved study staff performing study-related tasks will be permitted to view identifiable information – except where required by law.

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Personal information about you might be shared with or copied by authorized representatives from the following organizations for the purposes of managing, monitoring and overseeing this study (as required by law):

- The study sponsor, representatives of the sponsor and other collaborating organizations
- Representatives of VCU and the VCU Health System
- Officials of the Department of Health and Human Services

A description of this clinical trial will be available on http://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.

This study will **not** use your blood samples to sequence all or part of your DNA.

There are no plans to share any money or profits with you if the use of your sample(s) results in inventions or discoveries that have commercial value.

In the future, identifiers might be removed from the information you provide in this study (including results of the urine, blood, and breath analyses described above), and after that removal, the information could be used for other research studies by this study team or another researcher without asking you for additional consent.

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.

Important information about the availability of IQOS in the United States:

IQOS products have not been available in the United States since November of 2021 because of a patent dispute. IQOS is expected to be available for purchase in early 2023 (https://tinyurl.com/2s3a366f). At the conclusion of your participation in this study, if you express an interest in continuing to use IQOS, we will debrief you regarding the current (off the market) availability and expected near term availability (on the market) of

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IQOS. We will not provide any IQOS products for you to use apart from those require for completing the activities described in this study.

WHO SHOULD I CONTACT IF I HAVE QUESTIONS ABOUT THE STUDY?

If you have any questions, complaints, or concerns about your participation in this research, contact:

Dr. Andrew Barnes at 804-827-4361 / email: andrew.barnes@vcuhealth.org

The researcher/study staff named above is the best person(s) to call for questions about your participation in this study.

The medically responsible investigator is Dr. Thokozeni Lipato
thokozeni.lipato@vcuhealth.org

If you have general questions about your rights as a participant in this or any other research, you may contact:

Virginia Commonwealth University Office of Research
800 East Leigh Street, Suite 3000
Box 980568
Richmond, VA 23298
Phone: (804) 827-2157

Contact this number to ask general questions, to obtain information or offer input, and to express concerns or complaints about research. You may also call this number if you cannot reach the research team or if you wish to talk to someone else. General information about participation in research studies can also be found at http://www.research.vcu.edu/irb/volunteers.htm.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

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STATEMENT OF CONSENT

I have been provided with an opportunity to read this consent form carefully. All of the questions that I wish to raise concerning this study have been answered. By signing this consent form I have not waived any of the legal rights or benefits to which I otherwise would be entitled. My signature indicates that I freely consent to participate in this research study. I will have the opportunity to download a copy of the consent form for my records and/or receive a paper copy.

_____	
Adult Participant Name (Printed)	
_____	_____
Adult Participant's Signature	Date
_____	
Name of Person Conducting Consent Discussion (Printed)	
_____	_____
Signature of Person Conducting Consent Discussion	Date
_____	_____
Principal Investigator Signature (if different from above)	Date

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