Effects of Cigarette and E-cigarette flavors on Substitutability in the Experimental Tobacco Market Place

NCT05110872

03/05/2019

20-008 Effects of Cigarette and E-cigarette flavors on Substitutability in the Experimental Tobacco Marketplace

INSTRUCTIONS:

- *Use this "TEMPLATE PROTOCOL (HRP-503)" to prepare a study protocol outlining your research plan.*
- *Depending on the nature of your study, some major sections might not be applicable to your research. If so, simply mark as "N/A." For example, a simple survey might have many sections with "N/A." For subsections (e.g., 1.x or 8.x) you can mark as "N/A"if you are certain that the subsection is not applicable.*
- *Once the IRB/HRPP approves your submission, your latest approved version of the protocol will be stored in the IRB Protocol Management online system.*
- *If your research plan changes and you need to modify the protocol, please submit an amendment to Protocol Management with the requested modifications. Download your current protocol from Protocol Management and indicate the changes/revisions using the track changes feature in order to make review of the modifications easier to follow. If you are unable to use track changes, please create a new paragraph wherever you need to make a change, and indicate "Amendment: Date" before making a change to any section. Protocol management will store the older versions of your protocol if the IRB or HRPP staff need to compare them during the review.*

PROTOCOL TITLE:

Include the full protocol title.

Effects of filter ventilation and e-cigarette restrictions on cigarette demand and substitution in the Experimental Tobacco Marketplace

PROTOCOL NUMBER:

Include the number assigned in Protocol Management (verify this has been added before submitting protocol to HRPP).

VT IRB # 20-827

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FUNDING:

Sponsor(s): National Institutes of Health, National Cancer Institute - grant 5P01CA200512.
Funded already or in the proposal phase?: Funded
Is Virginia Tech the primary awardee or the coordinating center of this grant or contract? If not, list the primary institution: University of Minnesota. This

experiment is part of Project 3 of an NIH/NCI P01 Grant awarded to University of Minnesota (5P01CA217806-03). Virginia Tech is receiving a subcontract for Project 3. All of the human subject research activities for Project 3, including this experiment will be carried out by Virginia Tech.

VERSION NUMBER/DATE:

Include the version number and date of this protocol. Versions should start at 1.0.

Version 1.0 09/30/2020

REVISION HISTORY:

Use this table to keep track of changes. Add more rows as needed.

Revision #	Version Date	Brief Summary of Changes (i.e., the different sections)	Consent Change?

Table of Contents

1.0	Study Summary	4
2.0	Objectives	4
3.0	Background	5
4.0	Study Endpoints	10
5.0	Study Design and Statistical Analysis Plan	10
6.0	Setting	11
7.0	Study Intervention(s)/Investigational Agent(s)	12
8.0	Procedures Involved	13
9.0	Data and Specimen Long Term Storage and Use	17
10.0	Sharing of Results with Subjects	19
11.0	Study Timelines	19
12.0	Inclusion and Exclusion Criteria	19
13.0	Vulnerable Populations	20
14.0	Number of Subjects	21
15.0	Recruitment Methods	22
16.0	Withdrawal of Subjects	24
17.0	Risks to Subjects	24
18.0	Potential Benefits to Subjects	26
19.0	Data Management and Confidentiality	27
20.0	Provisions to Protect the Privacy Interests of Subjects	28
21.0	Provisions to Monitor the Data to Ensure the Safety of Subjects	30
22.0	Compensation for Research Related Injury	30
23.0	Economic Burden to Subjects	31
24.0	Consent Process	31
25.0	Process to Document Consent in Writing	34
26.0	Resources Available	35
27.0	Multi-Site Research	36

1.0 Study Summary

Study Title	Effects of filter ventilation and e-cigarette restrictions on cigarette demand and substitution in the Experimental Tobacco Marketplace
Study Design	This study uses a mixed design (within-subject repeated measures and between-group). Participants will be assigned to four different groups according to their preferred cigarette ventilation (ventilated and non-ventilated) and flavor (tobacco/menthol). Every participant will complete a few behavioral tasks, and make hypothetical purchases of tobacco products in an online store under four different scenarios: a) e-cigarette flavor restricted and e-cigarette nicotine restricted, b) e-cigarette flavor restricted and e-cigarette nicotine restricted, c) e-cigarette flavor restricted and e-cigarette nicotine restricted, d) e-cigarette flavor restricted and e-cigarette nicotine restricted.
Primary Objective	To examine the effects of filter ventilation and e-cigarette restrictions (on flavor and nicotine concentration availability) on cigarette demand and substitution in the Experimental Tobacco Marketplace
Secondary Objective(s)	N/A
Study Population	Cigarette smokers
Sample Size	268 completers
Research Intervention(s)/ Investigational Agent(s)	A survey consisting of questionnaires and behavioral tasks.
Study Duration for Individual Participants	This will be a one-session study that participants will complete remotely including consent, ETM purchases, and assessments (approximately 30 minutes).
Acronyms and Definitions	ETM: Experimental Tobacco Marketplace FBRI: Fralin Biomedical Research Institute VTCRC: Virginia Tech Corporate Research Center

2.0 Objectives

2.1 Describe the purpose, specific aims, or objectives of this study:

Purpose: To examine the effects of filter ventilation and e-cigarette restrictions (on flavor and nicotine concentration) on cigarette demand and the corresponding degree to which e-cigarettes and other non-combustible tobacco products substitute for cigarettes.

2.2 State the hypotheses to be tested:

This study is designed to better understand the effect of possible e-cigarette restrictions. We hypothesize that e-cigarette restrictions will decrease substitution for e-cigarettes, with the smallest degree of substitution when both flavors and nicotine concentration are restricted.

3.0 Background

3.1 Summarize the relevant prior research on this topic and gaps in current knowledge within the field of study:

The Food and Drug Administration (FDA) was granted authority in 2009 to establish tobacco product standards if those standards are reasonably expected to benefit the public health. One product feature that could be changed is cigarette filter ventilation. A recent review examined the effects of cigarette filter ventilation and concluded that filter ventilation, by changing how a cigarette burns, yields more mutagens and carcinogens, and results in greater puff volume and possibly depth of inhalation, which has led to increases in peripheral lung adenocarcinomas (1). This, along with the ability to manipulate systemic levels of nicotine by altering smoking behavior, as well as misconceptions about the lower toxicity of filter ventilation, may have also contributed to the use, appeal, and abuse liability of ventilated cigarettes. The extent to which commercial cigarettes are ventilated vary substantially in the market by brand, ranging from 0 to 80%. However, smokers compensate for the lower nicotine yields associated with higher ventilation by varying their puffing behavior, number of cigarettes per day, and blocking some portion of the ventilation holes. This compensatory behavior exposes smokers to more tobacco smoke constituents than would be indicated by machine smoking tests. Regulatory action that reduces or eliminates cigarette ventilation would not only reduce exposure to smoke constituents by increasing nicotine yield per cigarette, but also change the smoker's experience, likely resulting in harsher taste that may be proportional to the ventilation in a given cigarette brand. The potentially large effect on taste and preference corresponding to cigarette ventilation could alter the appeal and abuse liability of these products and could inform regulatory actions. However, eliminating filter ventilation raises a variety of questions that constitute a gap in our knowledge and must be answered to assess the potential for adverse unintended consequences of removing filter ventilation. We will explore these questions within a behavioral economic framework.

Behavioral economic demand analyses can be used to understand the level of motivation to consume a product on either an individual or small group level, including cigarettes (2,3). This level of analysis allows for experimental manipulations to be made on variables of interest. By quantifying how consumption decreases as costs increase to obtain and consume a product, important indices of demand are obtained. These indices can be grouped into two main measures of consumption, demand intensity and demand

elasticity, which are associated with use level and dependence severity (3,4,5,6). Demand intensity is the amount of the commodity consumed when available at very low cost (approaching free), and demand elasticity quantifies the degree to which the individual is willing to increase monetary or effort-based expenditures to maintain the same level of consumption as costs increase. Elasticity of demand has been shown to be a characteristic of the drug itself and independent of drug dose for many drugs including nicotine (2,7,8). While drug demand plotted as a function of unit price has been often shown to be a function of the total drug consumed, some of our prior research with cigarette demand calls this conclusion into question. A prior study we conducted (9) compared conventional cigarettes to denicotinized cigarettes. We found that, if these denicotinized cigarettes were the only tobacco product available, the denicotinized cigarettes had comparable demand to nicotinized cigarettes. If both were available, however, participants preferred the nicotinized cigarettes. This suggests that cigarette demand is not strictly regulated by nicotine dose, and that there is substantial abuse liability associated with other aspects of cigarettes (e.g., sensory components) apart from any nicotine content. Relevant to this point and the current application, we conducted a pilot study, where conventional ventilated cigarette smokers purchased either their usual cigarettes (ventilated) or their usual cigarettes with the filter vents blocked. When each cigarette type was available alone in separate sessions, demand for both products was very similar. However, in a separate session in which both cigarette types were available concurrently at equivalent unit prices, ventilated cigarettes were clearly preferred at all prices. These findings suggest that to fully understand the abuse liability of cigarettes will require that they are studied in contexts where other products are available (e.g., substitution).

Substitution is defined as an increase in the consumption of a constant-priced product while the cost of a different commodity is increased. For example, we have shown that as the price of conventional cigarettes is increased and its consumption decreased, the consumption of nicotine gum increased even though its price remained constant (10). Substitution defines one end of a continuum of interactions between two commodities. At the other end of that continuum, commodities can also function as complements. Complementarity refers to the decreased consumption of a constant-priced product in response to an increase in the price of a different commodity. For example, the research team has previously shown that as the price of cigarettes increased, consumption of coffee decreased even though its price remained constant (11). Between these two extremes is independence, which occurs when changes in the price of one commodity have little or no effect on consumption of another commodity where price has remained unchanged. Substitution, complementarity, and independence are measured by cross-price elasticity of demand and are represented by values that are positive, negative, or near zero, respectively. Studies to date have almost exclusively examined only pairs of products and, in even fewer cases, three concurrently available commodities. For example, in one of our studies smokers had access to conventional cigarettes, denicotinized cigarettes, and nicotine gum13. When the price of conventional cigarettes increased, consumption of both denicotinized cigarettes and nicotine gum increased even though their prices were fixed. Thus, denicotinized cigarettes and nicotine gum functioned as substitutes for conventional cigarettes. Indeed, by concurrently using both

products, the smoker could reproduce both the central and sensory effects of standard cigarettes by consuming the denicotinized cigarette (i.e., sensory effects) and nicotine gum (i.e., central effects). Importantly, denicotinized cigarettes functioned as a better substitute than gum (the use of denicotinized cigarettes increased the most). This effect could not have been predicted from the individual demand curves with these commodities. Only when they were measured together did these complex interactions emerge. Lastly, in this experiment consumption of conventional cigarettes was greatest when it was the only available product, and was least when denicotinized cigarettes or both alternatives were available. This finding demonstrates that cigarette demand was altered by the presence of alternative products and that under some conditions multiple products will be used concurrently. However, this and similar studies are constrained by arbitrary circumstances of the laboratory, such as required nicotine deprivation, constrained consumption of a product (e.g., 1 cigarette puff per self-administration), long and numerous sessions (e.g., one, 3-hour session for each price examined). As such, these methods cannot and do not come close to replicating the ever more complex tobacco marketplace and underscore the gap in the understanding of how to examine these relationships among a large number of products that approximate the real world.

To address this methodological gap and to inform how various products may interact, we have developed and tested a novel method called the Experimental Tobacco Marketplace (ETM). The ETM is a systematic extension of similar marketplace methods used with other consumer products (e.g., food marketplaces used in obesity and other nutrition-related research). In experimental marketplaces, multiple products are available and the experimenter controls the prices for each. These marketplaces can be either physical or virtual stores (similar to online retailers) and permit the examination of price effects and an assessment of degree of substitution or complementarity in consumer behavior under conditions that approximate naturalistic settings. One such study (12) examined foods purchased by mothers when less healthy foods were taxed (increased price) and healthier foods were subsidized (decreased price). These authors found that taxing less healthy food reduced caloric intake and proportion of calories from fat, while increasing the amount of protein consumed. Alternatively, subsidizing healthier foods did not change the macronutrient profile of foods purchased while increasing energy intake. In a review of this emerging area of nutritional research, Epstein and colleagues noted that “price changes modify purchases of targeted foods, but research on the overall nutritional quality of purchases is mixed because of substitution effects” (p. 789; (13)). This statement suggests the importance of exploring regulatory options in complex marketplaces. The ETM developed by the investigative team is similar to an online store, that displays pictures, information, and prices for several tobacco/nicotine products. In a recent study of ours (14), smokers were endowed with an amount of money comparable to their weekly tobacco purchases. They then made tobacco product purchasing decisions while the price of conventional cigarettes was varied and the price of 5 other tobacco products remained constant. Purchasing decisions from one, randomly selected cigarette price was actualized and smokers were provided the products purchased and any unspent account balance. Smokers returned one week later to report tobacco/nicotine use and return unused products for a refund. Cigarette consumption decreased as a function of price. As the price of cigarettes increased, consumption of snus, electronic cigarettes, and

nicotine lozenges showed the greatest substitution. Importantly, this approach moves beyond the constraints of previous laboratory studies by permitting the study of tobacco/nicotine preference and consumption under conditions that typically occur in most smokers' lives, including not being nicotine deprived, consuming the products in their natural environment, selecting the products they wish from a large number of products, and consuming the products while engaging in normal daily activities.

In this experiment, we will ascertain the impact of e-cigarette restrictions (on flavor and nicotine concentration availability) on cigarette demand and substitution in the ETM across a range of cigarette prices to model the effect of ventilation. We will assess these measures in each of four smoker subtypes: unventilated menthol smokers, ventilated menthol smokers, unventilated non-menthol smokers, ventilated non-menthol smokers. For this purpose, ventilated and unventilated cigarettes will be defined as ≥20% and <10% filter ventilation, respectively. Thus, in this experiment, we will examine whether the effects of e-cigarette restrictions differ by smoker subtype.

References

1. Song M, Benowitz N, Berman M, ...et al. Cigarettes filter ventilation and its relationship to increasing rates of lung adenocarcinoma (under review).
2. Bickel, W. K., DeGrandpre, R. J., Hughes, J. R. & Higgins, S. T. Behavioral economics of drug self-administration. II. A unit-price analysis of cigarette smoking. J. Exp. Anal. Behav. 55, 145–154 (1991).
3. MacKillop, J. et al. Further validation of a cigarette purchase task for assessing the relative reinforcing efficacy of nicotine in college smokers. Exp. Clin. Psychopharmacol. 16, 57–65 (2008).
4. Murphy, J. G., MacKillop, J., Tidey, J. W., Brazil, L. A. & Colby, S. M. Validity of a demand curve measure of nicotine reinforcement with adolescent smokers. Drug Alcohol Depend. 113, 207–214 (2011).
5. MacKillop, J. et al. Latent structure of facets of alcohol reinforcement from a behavioral economic demand curve. Psychopharmacology 203, 33–40 (2008).
6. MacKillop, J. et al. Alcohol demand, delayed reward discounting, and craving in relation to drinking and alcohol use disorders. J. Abnorm. Psychol. 119, 106–114 (2010).
7. Hursh, S. R. & Roma, P. G. Behavioral economics and empirical public policy. J. Exp. Anal. Behav. 99, 98–124 (2013).
8. Hursh, S. R. & Winger, G. Normalized demand for drugs and other reinforcers. J. Exp. Anal. Behav. 64, 373–384 (1995).
9. Shahan, T. A., Bickel, W. K., Madden, G. J. & Badger, G. J. Comparing the reinforcing efficacy of nicotine containing and de-nicotinized cigarettes: a behavioral economic analysis. Psychopharmacology 147, 210–216 (1999).
10. Johnson, M. W. & Bickel, W. K. The behavioral economics of cigarette smoking: The concurrent presence of a substitute and an independent reinforcer. Behav. Pharmacol. 14, 137–144 (2003).

11. Bickel, W. K., Hughes, J. R., De Grandpre, R. J., Higgins, S. T. & Rizzuto, P. Behavioral economics of drug self-administration. Psychopharmacology 107, 211–216 (1992).
12. Epstein, L. H., Dearing, K. K., Roba, L. G. & Finkelstein, E. The influence of taxes and subsidies on energy purchased in an experimental purchasing study. Psychol. Sci. 21, 406–414 (2010).
13. Epstein, L. H. et al. Experimental research on the relation between food price changes and food-purchasing patterns: a targeted review. Am. J. Clin. Nutr. 95, 789–809 (2012).
14. Quisenberry, A. J., Koffarnus, M. N., Hatz, L. E., Epstein, L. H. & Bickel, W. K. The Experimental Tobacco Marketplace I: Substitutability as a Function of the Price of Conventional Cigarettes. Nicotine Tob. Res.(2015). doi:10.1093/ntr/ntv230
15. Benowitz, N. L. & Others. Compensatory smoking of low-yield cigarettes. National Cancer Institute. Risks associated with smoking cigarettes with low machine yields of tar and nicotine. Smoking and Tobacco Control Monograph No 13, 39–63 (2001).
16. Frost, C. et al. The tar reduction study: randomised trial of the effect of cigarette tar yield reduction on compensatory smoking. Thorax 50, 1038–1043 (1995).
17. Robinson, J. C., Young, J. C., Rickert, W. S., Fey, G. & Kozlowski, L. T. A Comparative Study of the Amount of Smoke Absorbed From Low Yield ('Less Hazardous') Cigarettes Part 2: Invasive Measures. Br. J. Addict. 78, 79–87 (1983).

3.2 Describe any relevant preliminary data:

The Experimental Tobacco Marketplace (ETM) [6], a novel method recently developed, permits estimates of the effects of new policies and products on consumption and substitution in the tobacco marketplace. This methodology places the mix of products, prices, and specific policies under experimental control so as to provide estimates of novel policies obtained under conditions that simulate "real world" circumstances. This approach provides insight into how a given policy may alter consumption, preferences, and substitution among tobacco products. As part of this grant, one previous study has examined the effect of removing filter ventilation on nicotine product consumption. Preliminary analysis shows that exposure to unventilated cigarettes might decrease demand for ventilated cigarettes and increase substitution for unventilated cigarettes. The manuscript is currently in preparation.

6. Bickel WK, Pope DA, Kaplan BA, et al. Electronic cigarette substitution in the experimental tobacco marketplace: A review. Prev Med 2018;117:98–106. doi:10.1016/j.ypmed.2018.04.026

3.3 Based on the existing literature, provide the scientific or scholarly rationale for and significance of your research and how will it add to existing knowledge:

No study to date has experimentally examined the effects of e-cigarette restrictions on demand for unventilated and ventilated cigarettes and substitution for other tobacco products. The rationale for this specific proposal is to explore prospectively the possible consequences of e-cigarette restrictions on consumption and substitution with tobacco products among ventilated and unventilated smokers. The results might inform tobacco control policies.

4.0 Study Endpoints

*4.1 Describe the primary and secondary **study** endpoints. See links below for discussion of study endpoints and how they may differ from study objectives. These are most common in clinical trials but are sometimes applicable to other types of biomedical research, as well as social, behavioral, or educational research. See link below for a discussion.*

https://docs.google.com/document/d/1Wocz7K7a0hCQJPPO_khh5l1SQQjhGDDGHzcOPRHR5Tw/edit?usp=sharing

Substitutability: all groups will be compared to assess whether substitutability with tobacco products occurs as a function of different flavor and nicotine restrictions and cigarette price.

*4.2 Describe any primary or secondary **safety** endpoints. These should be included for all studies that are greater than minimal risk. (Minimal risk: The probability and magnitude of harm or discomfort anticipated in the research that are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.)*:

This study will recruit adults who regularly smoke cigarettes. This study's procedures are not designed to increase daily nicotine use and we do not anticipate any increased risk to participants directly from this study.

5.0 Study Design and Statistical Analysis Plan

5.1 Describe the basic study design/approach (e.g., qualitative study using five focus groups of first year students to describe assimilation into the university community; randomized controlled trial of a behavioral change intervention to increase dietary intake of whole grains; pre- post-test evaluation of new pedagogical techniques to improve adult literacy):

In a one-session study, participants will complete assessments and purchase tobacco products in a hypothetical ETM. All participants will complete four ETM conditions, all of which include five trials assessing different prices of their preferred cigarette. In each

ETM condition, participants will purchase tobacco/nicotine products for a 7-day period. Unventilated and ventilated cigarettes, as well as a range of other products (i.e., lozenges, snus, gums, and dip), will be always available. Availability of e-cigarettes will vary according to the following conditions:
A) Nicotine restricted and flavor restricted
B) Nicotine unrestricted and flavor restricted
C) Nicotine restricted and flavor unrestricted
D) Nicotine unrestricted and flavor unrestricted
Participants will be exposed to these restriction conditions across purchasing scenarios in a counterbalanced order.

5.2 Describe corresponding data analysis plan/approach (e.g., content analysis of focus group transcripts; descriptive analysis followed by linear regression modeling; nonparametric analysis of pre- and post-test measures):

The analysis of each group will assess whether substitutability occurs as a function of different e-cigarette conditions. The relationship between consumption and condition will be modeled according to:

$$y_{ij} = \mu + \alpha_i + \tau_j + \varepsilon_{ij},$$

where y_{ij} represents the average log consumption for the ith e-cigarette restriction and the jth subject, α_i is the effect of the ith condition on log consumption, τ_j is the effect of the jth subject, ε_{ij} is the error term, i=1, 2, 3, 4 and j=1,…,n.

Additionally, all the groups will be compared to assess whether substitutability occurs as a function of different e-cigarette conditions. The relationship between consumption and condition will be modeled according to:

$$y_{ijk} = \mu + \alpha_i * b_j + \tau_k + \varepsilon_{ijk},$$

where y_{ijk} represents the average log consumption by condition for the ith e-cigarette restriction, in the jth smoking status and the kth subject, α_i is the effect of the ith condition on log consumption, b_k is the effect of the jth group on log consumption τ_k is the effect of the kth subject, ε_{ijk} is the error term, i=1, 2, 3, 4, j=1, 2, 3, 4 and k=1,…,n.

Additional analyses might be conducted.

6.0 Setting

6.1 Describe the sites or locations where your research team will conduct the research. Consider each of the items listed below:

- *Identify where your research team will identify and recruit potential subjects.*
- *Identify where the team will perform the research procedures.*
- *Describe the composition and involvement of any community advisory board(s).*

- *For research conducted in other locations, describe:*
  - *Site-specific regulations or customs affecting the research at those locations.*
  - *Local scientific and ethical review structure at those locations. Examples include work in other cultures or ethnic groups (within or outside of the U.S.) and work with churches. The HRPP will provide additional guidance for international research.*

Recruitment: This study will use a contracted survey firm panel, Ipsos Public Affairs, LLC, which contains approximately 60,000 members via an address-based sampling methodology from the U.S. Postal Service's database. Adults from sampled households are invited to join this panel. Panel members will be recruited and screened by Ipsos Public Affairs, LCC to complete an online session.

Location of study: The research procedures will be performed remotely. The study consent and survey will be prepared by our VT team. Recruitment will be conducted by the Ipsos Public Affairs, LCC and closely monitored by our team. All participants will enroll on a voluntary basis and consent electronically prior to study participation.

7.0 Study Intervention(s)/Investigational Agent(s)

7.1 Describe the study interventions (including behavioral interventions) and/or investigational agents (e.g., drugs or devices) to be used in this study. Consider each of the items listed below:

- *Drug/Device Handling: If the research involves drugs or devices, describe your plans to store, handle, and administer the drugs or devices so that they will be used only on subjects, and only by authorized investigators.*
- *Describe whether any of the following will be used: microwaves, X-rays, DEXA scans, general anesthesia, or sedation*
- *If control of the drugs or devices used in this protocol will be accomplished by following an established, approved organizational SOP (e.g., Research Pharmacy SOP for the Control of Investigational Drugs, etc.), please reference the SOP in this section.*

This study does involve experimental manipulation of nicotine/tobacco product price and availability on a hypothetical online store to understand consumer's behavior. No drugs or devices will be provided to participants.

7.2 List the name of all drugs (including any vitamins, supplements, herbs, or nicotine) to be used in the study. Indicate whether they have FDA approval, and list any limitations for their use:

N/A

7.3 List all devices, how they will be used, their purpose in the study, and if they will be used in a manner consistent with their approved uses. If they will be used in ways that are not yet FDA approved, indicate whether they need an IDE or a determination that they are exempt from the IDE Determination. If a determination of significant risk or non-significant risk is needed for any of the devices, include the researcher's recommendation for each of those devices:

N/A

7.4 If the drug is investigational (has an IND) or the device has an IDE or a claim of abbreviated IDE (non-significant risk device), include the following information:

- *Identify the holder of the IND/IDE/abbreviated IDE.*
- *Explain procedures followed to comply with sponsor requirements for FDA regulated research for the following:*

	Applicable to:		
FDA Regulation	***IND Studies***	***IDE studies***	***Abbreviated IDE studies***
21 CFR 11	***X***	***X***	
21 CFR 54	***X***	***X***	
21 CFR 210	***X***		
21 CFR 211	***X***		
21 CFR 312	***X***		
21 CFR 812		***X***	***X***
21 CFR 820		***X***	

N/A

8.0 Procedures Involved

8.1 Describe and explain the study design:

This study uses a mixed design (within-subject repeated measures and between-group). In a one-session survey, participants will complete assessments and purchase tobacco products in a hypothetical ETM. All participants will complete four ETM conditions, all of which include approximately five trials assessing different prices of their preferred

cigarette. In each ETM condition, participants will purchase tobacco/nicotine products for a 7-day period. Unventilated and ventilated cigarettes, as well as a range of other products (e.g., lozenges, snus, gums, and dip), will always be available. Availability of e-cigarettes will vary according to the experimental conditions:
A) Nicotine restricted and flavor restricted
B) Nicotine unrestricted and flavor restricted
C) Nicotine restricted and flavor unrestricted
D) Nicotine unrestricted and flavor unrestricted

Participants will be exposed to these conditions across purchasing scenarios in a counterbalanced order.

We will assess these measures in each of four smoker subtypes: unventilated menthol smokers, ventilated menthol smokers, unventilated non-menthol smokers, ventilated non-menthol smokers. For this purpose, ventilated and unventilated cigarettes will be defined as ≥20% and <10% filter ventilation, respectively.

Every participant will complete questionnaires on a computer, tablet or cell phone.

8.2 Provide a description of:

- *All research procedures being performed*
- *If the study has more than one procedure, session, and/or subject population, describe each procedure, session, and/or study population separately. For complex studies, you are encouraged to include a figure or chart.*

Participants will complete a one session study including consent and behavioral tasks (ETM and smoking-related assessments).

A Qualtrics survey will administer:
1) the electronic informed consent;
Participants will read through the informed consent and consent will be implied with submission of the assessment at the end or the survey.
2) smoking-related assessments
a) timeline follow back, to assess previous month recent smoking, e-cigarette use and consumption of nicotine products, and to determine ETM budget
b) tobacco use history, exposure and preferences questions;
c) the Fagerstrom Test of Nicotine Dependence for cigarettes and the Heaviness of Smoking Index for e-cigarettes to assess dependence.
3) the ETM;
Participants will make hypothetical purchases of tobacco products to use throughout the next 7 days. Participants will complete a total of 20 purchasing trials each for 7 days' worth of products. They will be exposed to 4 conditions with their preferred cigarettes increasing in price. The following conditions will be presented in a randomized order:

Conditions		E-Cigarette	
		Nicotine restricted	Nicotine unrestricted
E-Cigarette	Flavor restricted	E-cigarette nicotine restricted and E-cigarette flavor restricted	E-cigarette nicotine unrestricted and E-cigarette flavor restricted
	Flavor unrestricted	E-cigarette nicotine restricted and E-cigarette flavor unrestricted	E-cigarette nicotine and unrestricted E-cigarette flavor unrestricted

In the E-Cigarette Flavor Restricted, only tobacco flavors will be available. In the E-Cigarette Flavor Unrestricted, a variety of flavors will be available. In the E-Cigarette Nicotine Restricted, only low nicotine concentration will be available. In the E- Cigarette Nicotine Unrestricted, a variety of nicotine concentration will be available.
A range of other tobacco products will be available across conditions, such as snus, lozenge, gum, and dip.

8.3 Describe:

- *Procedures or safeguards intended to reduce the probability and magnitude of risks. (For example: Reducing the risk of injury in a virtual reality study either by having the subjects sit during the study or by providing an obstacle-free space for walking.)*
- *Be sure to describe all drugs and devices used in the research, when they will be administered or used, and their purpose.*
- *Methods used to collect data about subjects. Please upload all data collection forms to Protocol Management. Some common examples are:*
  - *Screening questionnaires*
  - *Survey(s), including online surveys*
  - *Demographic questionnaire(s)*
  - *Interview guide(s), e.g., questions or pool of questions for semi-structured interviews*
  - *Focus group guide(s)*
  - *Other documents used to collect data*

Participation in this study is completely voluntary and participants may choose not to participate at any time.
Panel members from IPSOS Public Affairs, LLC complete profile surveys that contain demographic questions available to investigators. IPSOS will provide demographics data from study completers.

Specific information and data for this study will be collected from a self-reported survey. Examples of the assessments described in section 8.2 are attached.

8.4 What data will you collect during the study and how you will obtain them? Please include descriptions of electronic data collection, database matching, and app-based data collection:

All of the survey and questionnaire data will be collected using Qualtrics, an online survey platform used to develop, administer, and collect participant data in a secure password protected database.
All tasks can be performed on a computer, tablet or cell phone. Only study personnel will have access to the collected data.

8.5 Who will transcribe or code audio and/or video recordings?:

N/A

8.6 Include a description of any deception to be used in the study. Include justification for the use of deception (why the deception is necessary), describe the debriefing process, and describe how the study meets <u>all</u> the following criteria for alteration of consent (deception is considered an alteration of informed consent):

- *The research involves no more than minimal risk to the subjects*
- *The alteration will not adversely affect the rights and welfare of the subjects*
- *The research could not practicably be carried out without the alteration/deception*
- *(Optional but encouraged in most cases) Subjects will be provided with additional pertinent information after participation (i.e., debriefing for studies involving deception)*

N/A

8.7 If the study involves long-term follow-up (once all research related procedures are complete), describe what data will be collected during the follow up period and when it will occur:

N/A

9.0 Data and Specimen Long Term Storage and Use

9.1 If you will store data or specimens for future use, describe where you will store the data or specimens, how long they will be stored, and how and by whom the data or specimens will be accessed:

All participant electronic data, will be stored in secure places to protect confidential participant information. Secured places will include password-protected databases accessible only to study personnel. Additionally, all data will be backed up on secure password-protected servers. Moreover, all data will be quality controlled in preparation for data analyses.

Data collected from this study will be retained and destroyed in accordance with the center's policy that requires a 3-year retention period following final publication of the data.

IRB regulations will be strictly adhered to in the conduct of the proposed research. Specifically, prior to implementation of any protocol changes, amendments will be submitted to the IRB for approval.

9.2 For specimens, list the data to be stored or associated with each specimen:

N/A

9.3 Describe the procedures to release data or specimens outside of the research team, including the process to request a release, approvals required for release, who can obtain data or specimens, and what data will be provided with specimens:

Investigators will adhere to all NIH requirements regarding data sharing. Only de-identified participant data collected will be shared for analysis outside of the study team. As part of this process, all investigators will be required to agree to the following conditions: 1) will adhere to the reporting responsibilities; 2) will not redistribute the data beyond the requesting individual and named collaborators; 3) will give appropriate acknowledgement; 4) will not use the data for commercial purposes; and 5) will obtain appropriate ethical approvals.

Results from research conducted will be shared and disseminated, including: regular project meetings, annual meetings, symposia, workshops, and/or conferences for related groups. Manuscripts will be written and submitted for publication in peer-reviewed journals/conferences, following the NIH Public Access Policy guidelines. All necessary ethical approvals will be obtained.

Data requests will be reviewed by the principal investigator and data will be shared with the expectation of acknowledgment of funding source and primary study team.

9.4 Describe the identifiers to be included with stored data or specimens, as well as any key or code that could be used to make them identifiable. Describe where the code will be stored, who will have access to it, and when it will be destroyed:

The VTC study team will not have access to any identifiers. Participants will be recruited and assigned a study ID by IPSOS Public Affairs, LLC, that are thereafter associated with all collected data. The electronic de-identified data is stored on the shared servers which are password protected.

9.5 Please select the identifiers you will obtain (whether directly from participants or from another source), including but not limited to:

☐	*Name*
☐	*Geographical subdivisions smaller than a state, including street address, city, county, precinct, zip code, and equivalent geocodes (note, the initial three digits of a zip code are not considered identifiable)*
☐	*Elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death, and single year of age over 89 and all elements of dates (including year) indicative of such age (note, such ages and elements may be aggregated into a single category of age 90+)*
☐	*Phone numbers*
☐	*Fax numbers*
☐	*Electronic mail addresses (e-mail)*
☐	*Social Security numbers*
☐	*Medical record numbers*
☐	*Health plan beneficiary numbers*
☐	*Account numbers*
☐	*Certificate/license numbers*
☐	*Vehicle identifiers and serial numbers, including license plate numbers*
☐	*Device identifiers and serial numbers*

☐	*Web Universal Resource Locators (URLs)*
☐	*Internet protocol (IP) address numbers*
☐	*Biometric identifiers, including finger and voice prints (audio recording)*
☐	*Full face photographic images and any comparable images (including video recording)*
☐	*Student record number or identification number*
☐	*User name for online or computer accounts*
☐	*Any other unique identifying number, characteristic, or code (note this does not mean the unique code assigned by the investigator to code the data)***:** Click here to explain.

10.0 Sharing of Results with Subjects

10.1 Describe whether you will share results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) with subjects or others (e.g., the subject's primary care physician). If so, describe how you will share the results and include this information as part of the consent document. Upload materials you will use to explain the results to subjects:

We will not share study results or individual results directly with the study participants or others.

11.0 Study Timelines

11.1 Describe:

- *The duration of an individual subject's participation in the study (for example, 1 hour, 2-4 weeks, 3-5 years).*
- *The amount of time expected to enroll all study subjects (weeks, months, years, etc.)*
- *The amount of time expected for the investigators to complete this study including primary data analyses.*

Participant's schedule: the participation of one subject is expected to take approximately 30 minutes in a single session.

Study timeline: enrollment and data collection are expected to take about 1 month.

The study team has projected this study to take approximately 1 year to complete enrollment, data collection and data analysis.

12.0 Inclusion and Exclusion Criteria

12.1 Describe how you will screen individuals for eligibility. When will screening occur and what procedures will you use? Upload any screening scripts or surveys to Protocol Management:

Participants will be first screened by IPSOS Public Affairs, LLC, for regular tobacco use. Cigarette smokers will be invited to participate in this study and have access to a survey link. Participants will then be screened to verify specific eligibility criteria for this study with questions about number of cigarettes smoked per day and cigarette brand and type.

12.2 Describe the eligibility criteria that define who will be included and who will be excluded from enrollment for each procedure of your study. Include any geographic criteria (e.g., Virginia Tech undergraduate students, a national sample of adults with engineering degrees, minors aged 8-12 in the New River Valley, university faculty in Virginia and Paris, France):

Inclusion criteria for signing consent will require that participants:
Be at least 21 years old
Smoke cigarettes daily (≥ 10 cigarettes/day)
Smoke ventilated or unventilated cigarettes (≥20% and <10% filter ventilation, respectively)

There will be no additional exclusion criteria for this study.

12.3 Indicate specifically whether you will include or exclude each of the following special populations: (You may not include members of these populations as subjects in your research unless you indicate them in the description of your subject population.)

- *Minors, as defined by state law where the study is performed (infants, children, teenagers)*
- *Pregnant women (can be included in minimal risk studies by mentioning in section 13.1)*
- *Prisoners (including all incarcerated individuals)*
- *Adults not capable to consent on their own behalf*

This study will focus on cigarette smokers. We will not include individuals under the age of 21 in compliance with Federal law. Minors, prisoners, and adults not capable to consent on their own behalf will not be part of the recruitment. Pregnant women will not be excluded and might be invited for this study.

13.0 Vulnerable Populations

13.1 If the research involves individuals who are vulnerable to coercion or undue influence, please describe additional safeguards you will include to protect their rights and welfare. Consider the applicable items listed below:

- *If the research involves Virginia Tech students, indicate whether these are students of any of the investigators. If so, describe whether the activities will take place during class time as part of the curriculum and the steps you will take to reduce the possibility that students feel obliged to participate in order to improve their course grade. The HRPP can provide further guidance as needed. Describe whether you will request access to student records (e.g., SAT, GPA, GRE scores).*
- *If the research involves employees of Virginia Tech or the research sponsor, describe steps you will take to ensure that the employees are freely participating and describe how their data will be protected from inspection by their supervisors.*
- *If the research involves Virginia Tech NCAA athletes, you must obtain approval from the athletic department.*
- *For research involving Montgomery County Public Schools, you must obtain county approval (after obtaining contingent Virginia Tech approval). Other locales have different requirements; please check on these and describe here. Approval is typically granted by the superintendent, principal, and classroom teacher (in that order). Approval by an individual teacher is insufficient. School approval, in the form of a letter or a memorandum should be uploaded as a supporting document.*
- *If the research involves pregnant women, review "CHECKLIST: Pregnant Women (HRP-412)" to ensure that you have provided sufficient information in this protocol.*
- *If the research involves prisoners, review "CHECKLIST: Prisoners (HRP-415)" to ensure that you have provided sufficient information in this protocol.*
- *If the research involves persons who have not attained the legal age for consent to treatments or procedures involved in the research (minors), review the "CHECKLIST: Minors (HRP-416)" to ensure that you have provided sufficient information in this protocol.*
- *If the research involves cognitively impaired adults, review "CHECKLIST: Cognitively Impaired Adults (HRP-417)" to ensure that you have provided sufficient information in this protocol.*

Pregnant women might participate in the study if they meet the inclusion criteria, although pregnant women will not be directly recruited because of their status. There are no procedures in this study that can represent a threat to their rights or welfare.

14.0 Number of Subjects

14.1 Indicate the total number of subjects to be enrolled and how this number was determined (e.g., sample size calculation [show], number of available subjects in a finite pool, number of tests funding award would allow):

In this experiment, we request 268 participants for all four groups which will allow detection of effect size f=0.24 with 90% power using alpha =0.05 type I error rate and a within subject correlation of 0.5. According to Cohen's 1988 conventions, this is a medium effect size (f=0.24). This calculation was done using G*Power assuming a repeated measures ANOVA testing a within-between subject effect for the 4 conditions (e-cigarette flavor and nicotine restrictions).

Additionally, including all four groups together will provide more than sufficient power assuming a repeated measures ANOVA testing a within-between subject effect for 4 groups (between-factor; smoking preferences) and 4 conditions (within-subject; e-cigarette restriction).

14.2 If this is a multi-site study, indicate the number of subjects to be enrolled at this site and the total to be enrolled from all sites:

N/A

14.3 If applicable, indicate the number of potential subjects you expect to screen for enrollment, and the number of subjects you will need to complete the research procedures:

As stated previously, the survey will be conducted using the IPSOS web-enabled KnowledgePanel®, a probability-based panel designed to be representative of the U.S. population. We anticipate screening around 3,250 participants in order to complete a total of 268 participants.

14.4 If the study has more than one procedure, indicate the total number of subjects to undergo each procedure separately:

All participants will undergo one entire study session unless they withdraw consent.

15.0 Recruitment Methods

15.1 Describe when, where, and how you will recruit potential subjects:

The survey will be conducted using the IPSOS web-enabled KnowledgePanel®, a probability-based panel designed to be representative of the U.S. population. Initially, participants are chosen scientifically by a random selection of telephone numbers and residential addresses by IPSOS. Persons in selected households are then invited by telephone or by mail to participate in the web-enabled KnowledgePanel. For those who agree to participate, but do not already have Internet access, Ipsos provides at no cost a laptop/netbook and ISP connection. People who already have computers and Internet service are permitted to participate using their own equipment. Panelists are sent emails throughout each month inviting them to participate in research. Cigarette smokers will be invited to participate in this study and receive unique log-in information for accessing this study's survey online. Panelists will receive up to two (2) email reminders will be sent to non-responders to encourage response.

15.2 Describe the source of subjects (for example, clinic patients with specific conditions, students in the library, community members at a gathering, or members of a local gym):

As stated above, the survey will be conducted using the IPSOS web-enabled KnowledgePanel®, a probability-based panel designed to be representative of the U.S. population. Initially, participants are chosen scientifically by a random selection of telephone numbers and residential addresses by IPSOS.

15.3 Describe the methods that you will use to identify potential subjects:

IPSOS Public Affairs will first screen cigarette smokers based on the information on their KnowledgePanel. Participants that meet this criterion will receive an invite to participate in this study.

15.4 Describe materials that you will be use to recruit subjects. Attach copies of these documents with this protocol in Protocol Management and be sure to include the IRB protocol number on each document.

- *For flyers, attach the final copy of printed flyers.*
- *For Virginia Tech News, Facebook postings and ads, newspaper ads, websites, MTurk/SONA/online survey systems, etc., attach the final wording and graphics to be used.*
- *For email recruitments, please include the subject line.*
- *For advertisements meant for audio broadcast, please submit the wording of the advertisement prior to taping (to avoid having to re-record with approved language) and submit the final recorded version for IRB review before use.*
- *Describe any compensation to subjects. Separate compensation into appropriate categories, such as: reimbursement for expenses, time and*

effort, and additional incentives for study participation. For each category, specify the amount (including any pro-rated amount), schedule, and method of payment.

Recruitment email template is attached.

Participants will be paid through IPSOS Public Affairs, LLC upon completion of our survey. VT will pay the survey firm a flat rate per participant that we want to recruit. Participants are redirected to our study from the survey firms and after completion of our study, they are redirected back to the survey firms where they receive information about their remuneration and a reminder that they will be paid via existing survey firm infrastructure. Participants will receive from 5,000 points ($5 cash-equivalent) to 10,000 points ($10 cash-equivalent) for qualifying and completing a 30- or 40-minute survey depending on the median time of completion. These are the standard incentives for a survey of this length. It is possible that the panel firm recommend increasing the incentive in order to achieve targets if survey uptake is lower than anticipated.

16.0 Withdrawal of Subjects

16.1 Describe circumstances under which you anticipate subjects could be withdrawn from the research without their consent:

Every participant who gives their consent will have the opportunity to complete the study.

16.2 If applicable, describe any procedures for orderly termination (e.g., discontinuation of a study drug or debriefing after a behavioral intervention):

N/A

16.3 Describe procedures that you will follow when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection (e.g., participant declines to continue with regular blood draws, but continues with periodic behavioral questionnaires):

Participants can stop completing the survey without submitting it at any time. In this case, a participant will be withdrawn from the entire study.

17.0 Risks to Subjects

17.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related the subjects' participation in the research. Include for the IRB's consideration a description of the probability, magnitude, duration, and reversibility of the risks. Consider physical, psychological, social, legal, privacy, and economic risks. Do not indicate "No risk" or "N/A." Instead, for studies with very low risk (e.g., anonymous online questionnaire on a mundane topic) indicate "The investigators are not aware of any risks from participation in this study." or "No more than risks than are found in everyday life." The example consent form presents a tabular method for risk information, which you can also use here. Common risk types include:

- *Physical (e.g., potential for pain, discomfort, infection)*
- *Psychological (e.g., potential for stress, discomfort, and/or embarrassment)*
- *Social (e.g., potential for discrimination or stigmatization and disruption of personal and family relationships)*
- *Legal (e.g., potential for disclosure of illegal activity, negligence)*
- *Privacy (e.g., potential for personal information being accessed, used, or disclosed without the subjects' knowledge or consent, breach of confidentiality/security)*
- *Economic (e.g., potential for individuals to lose access to economic services, employment, insurability)*

There will be no direct costs for participation, although there are risks.

1. Possible embarrassment: This may result from answering questions that participant considers sensitive. Some of our questions will ask for information about substance use.

2. Possible discomfort: There is also the possibility that participant may become bored or frustrated during the research sessions.

3. Loss of confidentiality: The research team will employ every effort to maintain participant confidentiality, however the loss of confidentiality is a potential risk.

Due to the investigative nature of this study, there may be other risks that are currently unknown.

17.2 Indicate the measures you will use to minimize risks and monitor subjects for safety. (e.g., asking a subject at regular intervals to rate how they are feeling from 1 to 10, or to slowly crouch in order to check their balance.)

Informed Consent. All consenting methods will be conducted electronically using standard operating procedures. All participants will enroll on a voluntary basis and read

an IRB-approved consent form prior to study participation. Consent to participate in this study will be implied with submission of the assessment.

Protections against risk. Participants will be free to withdraw from the study at any time.

The risks enumerated above will be addressed by the following:
1. Possible embarrassment: Participants may discontinue at any time.

2. Possible discomfort: Participants can take breaks, if desired.

3. Loss of confidentiality: The use of study ID for participants will protect confidentiality. Password protected computer databases will have coded identifiers. Master databases linking subject names to study ID are only available through survey firm. VT will have no access.

17.3 If applicable, indicate which procedures might have risks to the subjects that are currently unforeseeable. This will be rare, and usually applicable when testing a new drug or device or a new use of an existing drug or device:

N/A

17.4 If applicable, indicate which procedures might have risks to an embryo or fetus should the subject be or become pregnant:

N/A

17.5 If applicable, describe risks to others who are not subjects (e.g., collection of sensitive health data that might affect sexual partners if disclosed, mandatory reporting of abuse, DNA testing that might affect family members or relationships):

N/A

18.0 Potential Benefits to Subjects

18.1 Describe the potential benefits that individual subjects might experience from participating in the research. Include the probability, magnitude, and duration of the potential benefits, as this will be useful to the IRB's risk:benefit analysis. Do not include benefits to society or others. Do not

list monetary or non-monetary compensation for participation, as this is not a benefit These should be included in section 2 or 3 of this document:

Participants will not directly benefit from participating in this study. However, the current study may help identify effective methods of assessing the use of tobacco products as well as policy changes, which may help the health of people in the future.

18.2 If applicable, specify that there are no anticipated direct benefits for participants:

There are no anticipated direct benefits for participation in this study.

19.0 Data Management and Confidentiality

19.1 Describe procedures that you will use for quality control to ensure validity of collected data:

The PI will oversee monitoring of the data collection procedures. These procedures will be reviewed regularly in a number of settings. For instance, issues pertaining to data validity and integrity will be addressed formally during regularly scheduled study personnel meetings in which all study personnel, including the PI, will be in attendance.

19.2 Describe any existing data or biospecimens you will obtain as part of this study. Include:

- *Variables or samples to be obtained*
- *Source of the data or specimens*
- *Your authorization to access or receive the data or biospecimens*
- *Whether the data or biospecimens are publicly available*
- *Whether the data or specimens you receive will contain identifiers*

Survey firm will only provide demographics data from completers. See "Standard Demographics" attached. No biospecimens will be obtained.

19.3 Describe the steps that you will take to handle and secure study data during data collection, storage, use, and transmission. Include information about training of study staff, authorization of access,

password protection, encryption, physical controls, certificates of confidentiality, separation of identifiers and data, etc.:

To secure study data computer databases will have coded identifiers, only ID numbers will be used and data will be kept in secure locations. Access to study data will be limited to study personnel who have completed the IRB Human Subjects Training and who have been delegated the responsibility of data collection, management, or analyses by the PI. In addition, this project is included in the NIH grants' certificate of confidentiality.

19.4 For multi-site studies, describe how data or specimens will be handled and secured for each site (e.g., central or disseminated data storage, data coordinating center):

N/A

19.5 Describe the plan for data disposition following the conclusion of the study (e.g., long term maintenance of data, data destruction methods).

- *What information will be included in the long term storage of data or specimens?*
- *How long will the data or specimens be stored?*
- *Where and how data or specimens will be stored?*
- *Who will have access to the data or specimens during long term storage?*
- *Who is responsible for receipt or transmission of the data or specimens?*
- *How will data or specimens be shared or transported?*
- *When and how will personal identifiers be destroyed?*

As stated previously, data collected from this study will be retained and destroyed in accordance with the center's policy that requires a 3-year retention period following final publication of the data.

20.0 Provisions to Protect the Privacy Interests of Subjects

20.1 Describe the steps that you will take to protect subjects' privacy interests. "Privacy interest" refers to a person's desire to place limits on with whom they interact or to whom they provide personal information (e.g., collecting the minimal amount of private information required to complete the study, protecting the data once it is obtained):

No private information will be collected in this study. Private information is collected and protected by IPSOS Public Affairs, LLC. Procedures to keep all other the information safe are described in section 9.4.

20.2 Describe steps that you will take to make subjects feel at ease with the research situation in terms of the questions being asked and the procedures being performed. "At ease" does not refer to physical discomfort, but the sense of intrusiveness a subject might experience in response to questions, examinations, and procedures (e.g., use of a same gender investigator to place sensors on the torso, a private changing area if clothing must be changed, sensitivity when discussing pregnancy testing with subjects, making it clear on surveys that participants can discontinue at any time, not asking questions about private or sensitive issues unless necessary for the research):

Participants will voluntarily complete the study in the place of their choice on their own time using a computer, tablet or cell phone. All participants are informed that their information is confidential.

20.3 Describe how you plan to access existing sources of information about the subjects (e.g., medical records, grades) and how you will protect participant privacy through the data security plan:

The VT team will provide IPSOS with study's IDs from participants that completed the survey. IPSOS will then provide demographics from their knowledge panel. No private information will be exchanged.

20.4 Describe any required reporting that might occur as a result of your research questions, study populations, and data collection methods. Examples for Virginia and Virginia Tech include:

- ***Any*** *suspicions (e.g., circumstantial, disclosed) of child abuse (physical, emotional, sexual) and neglect*
- *Sexual discrimination and/or sexual violence that involves a student*
- *Disclosure or signs of intention to harm oneself (i.e., suicidal ideation and/or plan)*
- *Disclosure or signs of desire to harm others (i.e., homicidal ideation and/or plan)*
- *Suspected abuse, neglect or exploitation of vulnerable adults (e.g., individuals with a disability, elderly persons)*

We do not expect any required reporting to occur as a result of our research questions and data collection methods.

21.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

Safety monitoring is <u>required</u> when research involves greater than minimal risk and is sometimes appropriate for other studies.

21.1 Describe:

- *The plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe (e.g., periodic reporting to the IRB, establishing a data monitoring committee, reporting data monitoring committee findings to the IRB and the sponsor).*
- *What data you will review, including safety data, unexpected events, and data that show the ability to produce the intended results.*
- *How the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with subjects).*
- *The frequency of data collection, including when safety data collection starts.*
- *Who will review the safety data and with what frequency.*
- *The statistical tests for analyzing the safety data to determine whether harm is occurring.*
- *Any conditions that will trigger an immediate suspension of the research (e.g., a serious adverse event).*

N/A

22.0 Compensation for Research Related Injury

22.1 If the research involves more than minimal risk to subjects, describe the available compensation in the event of research-related injury, if any:

N/A

22.2 Provide a copy of contract language, if any, relevant to compensation for research-related injury. At Virginia Tech, this is most common for sponsored research:

N/A

23.0 Economic Burden to Subjects

23.1 Describe any costs that subjects might be responsible for because of participation in the research, including any uncompensated costs for items such as transportation, missed work, and childcare:

There are no costs to participate in this study.

24.0 Consent Process

24.1 Indicate the process by which you will obtain consent for study participation. Please upload all consent, parental permission, and assent forms, documents, and scripts referenced in this section to Protocol Management.

Describe the following:

- *Where the consent process will take place (e.g., clinic waiting area, classroom, online)*
- *The time interval between sharing the consent information with the prospective subject and obtaining consent. For lab, interview, and focus group studies, the Virginia Tech IRB prefers that subjects have at least 24 hours to review the consent form and study information before the appointment where consent will be obtained. For simple online survey studies, you can typically present the consent information immediately before subjects begin participation.*
- *If applicable, processes to ensure ongoing consent or assent (e.g., for multiple sessions; for research in which a minor will turn 18 during the study; for longitudinal research with minors who will later be asked to provide or affirm their assent).*
- *Please review "SOP: Informed Consent Process for Research (HRP-090)" for recommended procedure. Describe your process, being sure to include:*
    - *The name and role of all study personnel who will be trained and certified by the PI to conduct the consent process*
    - *The time that will be devoted to the consent discussion*
    - *Steps that you will take to minimize the possibility of coercion or undue influence*
    - *Steps that you will take to gauge or ensure the subjects' understanding*

An invitation to participate in this study will be sent to participants during recruitment. If they are interested in completing the study, they will be provided with a link to the survey and will be able to read the informed consent and give their consent electronically.

Consent will take place on the internet and through the portal in which the survey will be administered. That is, we will include detailed information about the nature of the study prior to the assessment beginning. The potential participant will be instructed to read that information and by continuing with the assessment give consent. Furthermore, because we are obtaining the sample through a survey firm, these particular participants will have already been informed about this study and will have the opportunity to express interest or decline not only at the time the assessment is administered, but also when they are being recruited.

Non-English Speaking Subjects

- *Indicate what language(s) other than English are understood by prospective subjects or representatives.*
- *If non-English speakers will be recruited, describe the process you will use to ensure that the oral and/or written consent information provided will be in a language that they understand.*
- *If you translate consent forms and study materials, please provide a certified translation of the form as well as the certification document.*
- *Indicate the spoken language that study personnel obtaining consent will use. Describe how you will assess fluency of personnel obtaining consent to ensure that the translation is accurate.*

Non-English speakers will not be recruited.

Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)

- *Review the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" to ensure you have provided sufficient information for the IRB to make these determinations (i.e., that it meets the criteria for a waiver or alteration of the consent process).*

N/A

Subjects who are not yet adults (minors: infants, children, teenagers)

- *Describe the criteria that you will use to determine legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted (e.g., in Virginia, individuals under the age of 18 years).*

- *For research conducted in Virginia, review "SOP: Legally Authorized Representatives, Minors, and Guardians (HRP-013)" to determine which individuals in the state meet the definition of "minor."*
- *For research conducted outside of the state, please describe the legal requirements for the definition of "minor."*

- *Describe the process for obtaining parental permission.*
  - *Permission from one parent is acceptable for studies that involve no greater than minimal risk OR involve greater than minimal risk but present the prospect of direct benefit to the minor subject.*
  - *Permission from both parents is required in all other cases (unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the minor).*
- *Describe whether you will obtain permission from individuals other than parents or Legally Authorized Representatives, and if so, who will be allowed to provide permission. Describe the process you will use to determine these individuals' authority to consent to the minor's general medical care.*
- *Indicate whether you will obtain assent from all, some, or none of the minors. If you will obtain assent from some minors, indicate which minors will be required to assent. Consider chronological age and intellectual capacity when determining who will be required to provide assent (e.g., infants are unable to assent. However, teenagers are likely able to read and sign an assent form).*
- *When assent of minors is obtained, describe whether and how you will document it. Will minors sign an assent form or give verbal assent?*
- *Attach parental permission and minor assent forms or scripts in Protocol Management.*

N/A

Adults Unable to Consent

- *Describe the process you will use to determine whether an individual adult is capable of consent.*
- *List the individuals from whom you will obtain permission in order of priority (e.g., durable power of attorney for health care, court appointed guardian for health care decisions, spouse, and non-minor child).*
  - *For research conducted in the Virginia, review "SOP: Legally Authorized Representatives, Minors, and Guardians (HRP-*

013)" to determine which individuals in the state meet the definition of "legally authorized representative."
    - *For research conducted outside of Virginia, please describe the legal requirements for obtaining permission from a legally authorized representative in the state where the research will occur.*
- *Describe the process for assent of the subjects.*
    - *Indicate whether you will require assent from all, some, or none of the subjects. If some, indicate which subjects will be required to assent and which will not.*
    - *If you will not obtain assent from some or all subjects, please provide justification for not obtaining assent.*
    - *Describe whether and how you will document assent.*

N/A

25.0 Process to Document Consent in Writing

25.1 Consult "SOP: Written Documentation of Consent (HRP-091)" for recommended procedures, and describe whether and how consent of the subject will be documented in writing:

Consent will not be documented in writing.

25.2 If the research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, you can request that the IRB waive the requirement to obtain written documentation of consent (e.g., consent to participate is indicated by pressing a button for an online questionnaire – after the consent information is presented and before the questionnaire begins):

As stated above, consent will take place on the internet and through the portal in which the survey will be administered. That is, we will include detailed information about the nature of the study prior to the assessment beginning. The potential participant will be instructed to read that information and by continuing with the assessment give consent.

25.3 If you will document consent in writing, attach a consent document with places for signatures. If you will obtain consent, but not document consent in writing, please attach the consent script or text. Review "CHECKLIST:

Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information. You should use "TEMPLATE CONSENT DOCUMENT (HRP-502)"to create the consent document or script:

Electronic informed consent is attached.

26.0 Resources Available

26.1 Describe the resources available to conduct the research. For example, as appropriate:

- *Describe the PI's availability to supervise the research.*
- *Justify the feasibility of recruiting the required number of suitable subjects within the agreed recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?*
- *Describe the time that you will devote to conducting and completing the research.*
- *Describe your facilities.*
- *Describe the availability of medical or psychological resources that subjects might need as a result of an anticipated or unanticipated consequence of participation in the research.*
- *Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions (e.g., training plans, detailed study notebooks).*

The organizational structure of the study team involves overall leadership by Dr. Warren Bickel, who will assume full responsibility for all aspects of the project, including design and participant eligibility. Dr. Bickel will oversee study procedures. He will also oversee and delegate to the Co-Investigators and other study team members the responsibility of monitoring data collection. Behavioral data analysis will be overseen by Dr. Bickel and conducted by the Co-Is and the Statistician.

All staff involved in planning and monitoring of this study will have completed the IRB Human Subject Protection Training and Good Clinical Practice Training. Documentation of training will be maintained.

Participants will be recruited through a survey firm panel which contains approximately 60,000 members via an address-based sampling methodology from the U.S. Postal Service's database.

All methods and measures will be conducted using standard operating procedures. All participants will enroll on a voluntary basis and read an IRB-approved consent form prior to study participation. Consent to participate in this study will be implied with submission of the assessment.

This survey will be administered remotely and participants will not be required to visit our facilities.

Study team meet on a regular basis and any issues will be discussed and addressed all study personnel, including the PI.

27.0 Multi-Site Research

Contact the HRPP for multi-site research (involving multiple institutions) and the details required for this section will be provided. Otherwise, indicate N/A.

N/A

20-008 Effects of Cigarette and E-cigarette flavors on Substitutability in the Experimental Tobacco Marketplace

Principal Investigator: Warren K. Bickel
IRB# and Title of Study: 20-827
Sponsor: NIH/NCI

You are invited to participate in a research study. This form includes information about the study and contact information if you have any questions.

WHAT SHOULD I KNOW?

This survey is being conducted by the Addiction Recovery Research Center at the Fralin Biomedical Research Institute at Virginia Tech Carilion. The study will help researchers understand choice behavior in buying different types of tobacco and nicotine products.

If you decide to participate in this study, you will complete a survey. As part of the study, you will complete questions about:

your current tobacco/nicotine use and preferences

how you might purchase tobacco/nicotine products under different scenarios. You will be asked to browse our online store of tobacco/nicotine products and make a series of hypothetical purchases under different price scenarios. Although the purchases you will make in the study are not real, please answer all questions as if you were actually making the purchases. When completing these questions, you will only be able to enter in numbers using your keyboard.

The study should take approximately 30 minutes of your time, and you'll receive 5,000 bonus points if you qualify and complete the survey.
We do not anticipate any risks from completing this study.

You can choose whether to be in this study or not. If you volunteer to be in this study, you may withdraw at any time without consequences of any kind. The investigator may withdraw you from this research if circumstances arise which warrant doing so.

CONFIDENTIALITY

Your responses are anonymous. No personally identifiable information will be provided to Virginia Tech.

Any data collected during this research study will be kept confidential by the researchers.

WHO CAN I TALK TO?

If you have any questions or concerns about the research, please feel free to contact the KnowledgePanel Panel Member Support at 800-782-6899. You are not waiving any legal claims, rights or remedies because of your participation in this research study. If you have questions regarding your rights as a research participant, contact the Virginia Tech HRPP Office at 540-231-3732 (irb@vt.edu).
Your consent to participate in this research is implied with submission of the assessment.

Please print out a copy of this information sheet for your records.