Document Coversheet

Study Title:

Effects of Tobacco Flavoring and Liquid Composition on Vaping Topography

Institution/Site:	Roswell Park Comprehensive Cancer Center
Document (Approval/Update) Date:	01/03/2024
NCT Number:	NCT05876091
IRB Number	I 3234822

PROTOCOL TITLE:

Effects of Tobacco Flavoring and Liquid Composition on Vaping Topography

PROTOCOL NUMBER:

I-3234822

PRINCIPAL INVESTIGATOR:

Richard O'Connor, PhD
Roswell Park Comprehensive Cancer Center
Elm and Carlton Street
Buffalo, New York 14263
716-845-4517
Richard.O'Connor@RoswellPark.org

VERSION NUMBER: 2

DATE: 16NOV2023

SPONSOR: Roswell Park Comprehensive Cancer Center

FUNDING: NCI (5U54CA228110)

Confidentiality Statement

Table of Contents

1 OBJECTIVES

The ***premise*** of this study is that flavors or synthetic nicotine might be related to the phenomenon of 'indirect' toxicity. That is, regardless of whether the compounds show evidence of toxicity in a biological sense, they may nonetheless increase harm by other means, such as altering vaping topography (puffing) patterns, increasing appeal, decreasing risk perceptions, or masking harshness or irritation that might lead users to discontinue use.

1.1 Primary Objectives

- Examine the influence of tobacco flavoring composition on vaping topography
- Examine the influence of synthetic vs. tobacco derived nicotine on vaping topography

1.2 Secondary Objectives

- Examine differences in sensory and subjective effects by tobacco flavoring composition
- Examine differences in sensory and subjective effects by synthetic vs tobacco derived nicotine

1.3 Exploratory Objective

- To generate a cell line/tissue from optionally provided oral cell samples to demonstrate the feasibility of cell line/tissue generation and later, expose oral cells to the study products or product constituents to examine the cellular-level effects of the study products and their components.

2 BACKGROUND

To appreciate the potential role of flavor perception in the use of tobacco products, it is instructive to look at the broader literature on subjective effects and responses to the sensory properties of tobacco products. In general, tobacco products were designed in part with sensory factors in mind, in order to maximize appeal to different market segments (1-4). Rees et al. (5) suggest a framework of consumer response that groups responses into two broad classes: response to the product, including drug effects and sensory perceptions; and perceptions of messaging around that product, including advertising and packaging. Much of this literature is focused on cigarettes given their greater prevalence but is nonetheless instructive for examining other tobacco products. Sensory blockade reduces urge to smoke, providing indirect evidence for the importance of sensory factors in maintaining behavior (6, 7), and a body of work has attempted to dissociate the sensory and drug components of smoking (8-14). Flavors may also influence expectancies around tobacco products. Expectancies of positive sensory effects of smoking (e.g., look, feel, and taste) are predictive of smoking behavior and willingness to try different types of cigarettes (15-21).

Understanding how nicotine vaping products (NVP) are used by consumers in the real world is an important component of properly assessing their individual and population level health impacts. While not as extensively studied as cigarette smoking topography, vaping topography has been shown to vary as a function of product design (Hiler et al., 2020 (22); Spindle et al., 2018 (23); Kimber et al., 2021(24)) and to be related to aldehyde emissions (Talih et al., 2015 (25); Son et al., 2020 (26)). From a regulatory perspective, understanding patterns of puffing (vaping topography) is crucial to informing standardized vaping regimens, which can be used to compare products across brands and classes. A total of 32 studies published between 2013 and April 2021

have directly measured NVP puff topography, and reported mean values for key topography parameters (puff duration, volume, flow rate, interval). CORESTA protocols (3s, 55mL, 18.33 mL/s, 30 s interval) commonly underestimated puff volume and flow rate, for example, for NVP-experienced users (112.15±18.9 mL, 37.94±7.67 mL/s) and open NVPs (112.98±20.97 mL, 40.65±8.57 mL/s). Underestimation of puffing parameters such as puff volume may lead to underestimation of NVP nicotine and toxicant yields, causing miscommunication of information to consumers and regulators. Additional research is necessary to determine whether flavoring chemicals or type of nicotine used in the product are further confounds for measuring vaping topography.

3 INCLUSION AND EXCLUSION CRITERIA

3.1 Inclusion Criteria

To be included in this study, subjects must meet the following criteria:

1. Age ≥ 21 and ≤ 55 years.
2. Current daily vapers of products containing nicotine.
3. No daily concurrent use of other tobacco products.
4. Self-reported general good health.
5. Women of childbearing potential must be willing to provide a urine sample and test negative prior to receiving any study-related products/procedures.
6. Ability to speak, read, and write in English.
7. Participant must understand the investigational nature of this study and sign an Independent Ethics Committee/Institutional Review Board approved written informed consent form prior to receiving any study related procedure.

3.2 Exclusion Criteria

Subjects will be excluded from this study for the following:

1. Allergies - active untreated seasonal allergies that would interfere with smell or taste procedures.
2. Self-reported taste or smell deficits.
3. Pregnant or nursing female participants.
4. Medications known to interfere with taste/smell (i.e., certain nasal sprays, nasal antihistamines, decongestants, antibiotics, medications containing zinc).
5. Unwilling to use open system vaping device in laboratory setting.
6. Positive diagnosis of COVID-19 within 10 days prior to start of study intervention.
7. Unwilling or unable to follow protocol requirements.
8. Any condition which in the Investigator’s opinion deems the participant an unsuitable candidate to receive the study intervention.

3.3 Special Populations

The following special population groups are EXCLUDED from participation:

- Cognitively impaired adults/adults with impaired decision-making capacity
- Individuals who are not yet adults (infants, children, teenagers)
- Pregnant women
- Prisoners
- Adults aged 18-20 unable to legally purchase tobacco in New York State

3.4 Inclusion of Women and Minorities

Both men and women and members of all races and ethnic groups are eligible for this study.

4 LOCAL AND STUDY-WIDE NUMBER OF SUBJECTS

A maximum of 72 evaluable participants from the general population in the greater Buffalo area and Rochester will be enrolled.

5 LOCAL AND STUDY-WIDE RECRUITMENT METHODS

Adult participants are recruited by offered continuation of another study and local advertising. We will recruit via community events, contacts, ad postings in local daily, weekly, and college newspapers, websites such as Craigslist, any social media networks (i.e.: Facebook, Instagram, Twitter, Snapchat, etc.), local tobacco control networks (methods we have previously used to recruit successfully), television, and radio (see **Appendix A** for example).

Participants will be recruited from the general population, not from within the RPCI or URMC patient populations.

Participants will be compensated via 1) an Amazon Gift Card Code sent to their provided email (all sites), 2) direct deposit (URMC only), or 3) a physical Visa Gift Card (URMC only). A gift card code/deposit/card reload notification will be sent within 24-48 hours of the session completion. Funds (via Amazon Gift Card Code) are immediately available when added to their Amazon account and participants can check their balance as desired. This system will allow frequent, immediately available payments. Compensation will be given on an escalating schedule upon successful completion of each session. A $50 bonus will be given upon successful completion of all seven sessions. The escalating compensation schedule will be as follows:

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

6 MULTI-SITE RESEARCH

University of Rochester Medical Center (URMC) will be an additional study site. The site PI is Dr. Deborah Ossip. A reliance agreement will be entered wherein Roswell Park is the IRB of record. It is the responsibility of the Principal Investigator to ensure that:

- All sites have the most current version of the protocol and consent document.
- All required approvals (initial, continuing review and modifications) have been obtained at each site (including approval by the site's IRB of record).
- All modifications have been communicated to sites, and approved (including approval by the site's IRB of record) before the modification is implemented.
- All engaged participating sites will safeguard data, including secure transmission of data, as required by local information security policies.
- All local site investigators will conduct the study in accordance with applicable federal regulations and local laws.
- All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.

7 STUDY TIMELINES

Participants will complete up to 7 laboratory visits (approximately 1½ hour/visit) over about a 3 month period. Each visit will be scheduled a minimum of 24 hours and a maximum of 1 week apart. The time between visits may be extended up to 14 days (2 weeks) due to participant illness (e.g., COVID, influenza).

The total duration of the recruitment is 18 months with an approximate study completion date of 8-31-2024.

8 STUDY ENDPOINTS

8.1 Primary Endpoints

The primary endpoints are measures of vaping topography [(per-puff volume, inter-puff interval, peak flow rate, puff count, total volume (sum of volumes across all puffs)], which are treated as quantitative outcomes and will be summarized by:

- Condition (flavor or nicotine composition) and,
- Bout (directed or ad-lib) using the appropriate descriptive statistics.

8.2 Secondary Endpoints

The same type of modeling employed for the primary endpoints will be used to evaluate the effect of flavoring and nicotine formulation on sensory and subjective measures, such as:

- Sensory measures – irritation, harshness
- Drug effects – liking.

8.3 Exploratory Endpoint

- Oral cell samples will be used for cell line/tissue generation to examine the cellular-level effects of the study products and their components.

9 DESIGN

This is an open-label, factorial multi-center study of e-liquid composition and effects on vaping topography.

10 STUDY INTERVENTION

Participants will vape twice per session – once directed and once ad lib. In the directed bout, participants are instructed to take a 4 second puff on the device every 60 seconds until a total of 8 puffs are completed. In the ad lib bout, participants are free to puff as they like for a defined 15 minute period.

10.1 Duration of Treatment

Participants may remain on study and continue to receive study product in the absence of unacceptable toxicity or withdrawal from study, intercurrent illness that prevents further participation, participant demonstrates an inability/refusal to comply with study procedures or, participant withdraws from study.

10.2 Compliance

Compliance is assessed in the laboratory by trained research assistants. As participants only use the study products on site in the laboratory, participant noncompliance with product use is expected to be negligible.

11 PROCEDURES INVOLVED

11.1 Participant Registration

Eligibility of each participant will be established prior to registration.

Informed consent MUST be completed prior to receiving any study related procedures.

11.2 Screening

Participants will be screened for eligibility and scheduled via telephone by the study coordinator.

Screening will take approximately 15 minutes. Please see **Appendix B1** and **Appendix B2** for specific screening questions.

There are up to 7 laboratory sessions of up to approximately 90 minutes each. Participants will be scheduled at their convenience with a minimum of 24 hours and maximum of 1 week (2 weeks if participant illness occurs) between sessions. See Table 1 for an overview of study measures/samples.

11.3 Session Procedures

Once a participant is identified as eligible, a visit date and time will be scheduled.

Participants will complete all experimental conditions, and are to abstain from vaping for a minimum of 30 minutes prior to the study session.

The order of completion of Sessions 2-5 and 6-7 will be determined using Latin Square and A/B designs, respectively. Order of ad lib and directed bouts within a session will be determined by A/B designs.

Each laboratory session is expected to take approximately 90 minutes.

Directed vs. ad lib bouts. In the directed bout, participants are instructed to take a 4 second puff on the device every 60 seconds until a total of 8 puffs is reached. In the ad lib bout, participants are free to puff as they like for a defined 15 minute period.

Priming / Habituation Puff: At the beginning of each session, participants will take 1 priming puff and 1 habituation puff at a setting of 10 watts. If 10 watts is too harsh for the participant, wattage may be reduced by 2 until comfort level is obtained. Final wattage will be recorded and used throughout the session.

Session 1: Vaping topography using own-brand liquid

In this condition, we will use an A/B design to compare directed vs ad lib vaping of the participant's preferred product. After each bout, participants will complete a battery of sensory outcome measures. All questionnaires will be administered by the experimenter. Vape assembly and puffing regimen will also be directed by the experimenter. The device used will be a SmokTech® NORD2 or equivalent device. This session will be approximately 90 minutes long.

Sessions 2-5: Relationship of tobacco flavor formulation to vaping topography and sensory evaluation.

In this condition, we will use a 4 (flavor) x 2 (ad lib vs directed) within-subjects design. All liquids will have a 60/40 carrier concentration and 5% nicotine. Three commercial tobacco flavor variants versus one unflavored liquid (EC Blend) will be tested.

Over 4 laboratory sessions (sequence determined by Latin square), participants will complete ad lib and directed bouts (sequence determined by A/B design) using each flavor. After each vape, participants will complete a battery of sensory outcome measures. All questionnaires will be administered by the experimenter.

Vape assembly and puffing regimen will also be directed by the experimenter. The device used will be a SmokTech® NORD2 or equivalent device. These sessions will be approximately 90 minutes long.

Sessions 6-7: Relationship of nicotine formulation to vaping topography and sensory evaluation.

In this condition, we will use a 2 (nicotine form) x 2 (ad lib vs directed) within-subjects design. All liquids will have a 60/40 carrier concentration and 5% nicotine. The primary comparison is between 5% synthetic nicotine and 5% tobacco-derived nicotine.

Over 2 laboratory sessions (sequence determined by A/B design), participants will complete ad lib and directed bouts (sequence determined by A/B design) using each liquid form. After each vape, participants will complete a battery of sensory outcome measures. All questionnaires will be administered by the experimenter.

Vape assembly and puffing regimen will also be directed by the experimenter. The device used will be a SmokTech® NORD2 or equivalent device. These sessions will be approximately 90 minutes long.

11.4 Study Measures

Table 1 provides a summary of the study assessments and procedures.

Table 1 Study Measures

Reason	Measure	Visit	
		1	2-7
Indicators of individual differences	Phenylthiocarbamine (PTC)	1x / screening	
	6-n-Propylthiouracil (PROP)	1x / screening	
	Sodium benzoate tasting	1x / screening	
Pregnant or nursing females excluded from study participation	Urine pregnancy test for women of child bearing potential	1x / screening	
Preference Probes	Personal Food Taste Preferences	1x / session start	
Vaping Dependence	Penn State Dependence Scale	1x / session start	
Positive and Negative Affect	PANAS	1x / session start	1x / session start
Preference of large vs small reward	Delay Discounting	1x / session start	1x / session start
Base Sensory Measures	Self-Rated Sensory Ability	1x / session start	1x / session start
	Sensory e-cig Experiences Scale	1x / session start	1x / session start
	PROMIS-E	1x / session start	1x / session start
	SHRI-E	1x / session start	1x / session start
Sensory Impact	Generalized Magnitude Scale	2x / after each use	2x/ after each use

Reason	Measure	Visit	
		1	2-7
Upper airway sensation and subjective effects	Duke Sensory Scale	2x / after each use	2x / after each use
	Hedonic Attribute Profile	2x / after each use	2x / after each use
	Drug Liking Effects	2x / after each use	2x / after each use
	Product Evaluation Scale	2xs / after each use	2xs / after each use
Nicotine and Cotinine	Saliva	1x beginning of session & 2x / after each use	1x beginning of session & 2x / after each use
Oral microbiome assessment	Optional Oral Rinse Sample (Roswell Park Site only)	1x	

Sensory Acuity Screening

Prospective participants will complete phenylthiocarbamine (PTC), 6-n-propylthiouracil (PROP), and sodium benzoate tasting, commonly used indicators linked to individual differences (27), using manufactured, pre calibrated strips.

Urine

Female participants will be asked to urinate in a sterile 90-mL urine specimen container which will be tested for pregnancy.

Saliva Samples

Saliva samples will be collected before and after product use in both session using a Salimetrics SalivaBio Passive Drool method (https://salimetrics.com/collection-method/passive-drool-salivacollection- device/). This method involves unstimulated collection of whole saliva which will be passively drooled into a cryovial until ~1.8mL of saliva is collected. Samples will be divided into aliquots and frozen at -20 C. Saliva will be tested for nicotine using a GC-qTOF-MS method. Saliva will be further tested for stress markers of cortisol (https://salimetrics.com/assay-kit/salivary-cortisol-elisa-kit/) and DHEA (https://salimetrics.com/assay-kit/salivary-dhea-elisa-kit/) and proinflammatory cytokines of IL-6 (https://salimetrics.com/assay-kit/salivary-il-6-elisa-kit) and IL-1b (https://salimetrics.com/assaykit/salivary-interleukin-1-beta-elisa-kit/). Color intensity will be read at 450nm using a plate reader (BioTek). The integrated values of known standards will be used to generate a standard curve. Density values for unknown samples will be determined by interpolation from the standard curve for each analyte to calculate concentrations in pg/mL saliva. Saliva samples may also be used to test for nicotine and cotinine levels using similar methods to blood analyses. Additional details about the processing of saliva samples are

provided in **Section 15**. A full description of the sample collection procedure can be found in **Appendix D**.

Optional Oral Rinse Sample (Roswell Park site only)

Oral rinse samples will be collected using a rinse & gargle method with Scope mouthwash, which will be stored in a -80ºC freezer and kept at Roswell Park for analysis. We will characterize the microbiota by analyzing 16S rRNA (bacteria) and ITS1 gene (fungi) and the virome (including human papillomaviruses) using NGS. We will also complement analyses with functional information obtained through Bioinformatic algorithms (PICRUSt) and shotgun metagenomics. This approach will quantify differences in secreted and other microbial gene products; connect them to annotated pathways and make them available for downstream analyses. Thus, we will analyze inferred biochemical functions that are related to inflammation and subsequent oral and respiratory outcomes. Additional details about the processing of oral cell samples are provided in **Section 15**. A full description for oral rinse sample collection is provided in **Appendix D**.

eTop Vaping Topography

The eTop (American University of Beirut) is a mouthpiece-based desktop device designed to measure e-cigarette puff topography. eTop mouthpieces can be adapted for various e-cigarette designs. The eTop continuously monitors, digitizes, and records airflow through the mouthpiece that is connected to an e-cigarette. A puff is detected by a pressure transducer whenever changes in pressure occur across an orifice that is incorporated into the mouthpiece (e.g., when user begins to inhale). Orifice dimensions and transducer sensitivity provide valid measurements at puff flow rates as low as 3ml/sec. The signal from the transducer is digitized using a National Instruments data acquisition device (NI DAQ USB-6008) and communicated to the computer via USB. Data are stored offline by an associated computer application that communicates with the eTop device. Based on the start and end time of every puff, the total number of puffs detected, and the volume of each puff detected, the average puff duration (sec), interpuff interval (sec), puff volume (mL), and puff flow rate (mL/s) are computed. The eTop has been shown to capture topography data with high validity and reliability and does not interfere with natural e-cigarette puffing behavior (Felicione et al., 2020 (28)).

Sensory Measures

The product evaluation scale, Duke Sensory Scale, and Hedonic Attribute Profile will be used to examine different aspects of upper airway sensation and subjective effects. A labeled generalized magnitude scale will be used to score sensory impact. The sensory e-cig experiences scale; PROMIS-E; SHRI-E are also assessments that will be used. Refer to **Appendix C**.

Purchase Decision Making

We will administer a 5-trial adaptive delay discounting task, implemented in REDCap, to assess user preference for smaller immediate rewards over larger delayed rewards (i.e., delay discounting). This interactive instrument automatically adjusts to respondents' choices to produce a *k*-parameter after five trials. Participants are asked on the first trial whether they would prefer to receive $500 now or $1,000 in 3 weeks. If the immediate choice is selected ($500 now), then the second trial shortened the delay (i.e., choice: $500 now or $1,000 in 1 day). If the delayed option was chosen on the first trial ($1000 in 3 weeks), then the second trial lengthens the delay (i.e., $500 now or $1000 in 2 years). All subsequent trials are adjusted based on responses from the preceding trial. The *k*-parameter is expressed as the natural logarithm of *k* in a hyperbolic model,

with *k* increasing as the preference for smaller sooner rewards increases.(29) Additional items probe participants' reliance of various sources of information that may influence purchases.

Other Questionnaires

The PANAS is administered to probe current balance of positive and negative affect. Additional items probe personal food taste preferences. All of these will be explored as potential covariates for sensory ratings. The Penn State Dependence Scale will evaluate vaping dependence. Refer to **Appendix C**.

12 WITHDRAWAL OF SUBJECTS

Participants will be given phone numbers for research associates and supervising physicians to call if there are adverse effects or other study-related problems. Participants will be advised that if they have any adverse effects and/or wish to stop participating in the study for any reason, they are free to do so.

Participants who are injured as a result of being in the study will have treatment available. The costs of such treatment may be covered by Roswell, depending on a number of factors.

Any participant who discontinues due to an adverse event or adverse experience (AE) must be followed until the event resolves or stabilizes. Appropriate medical care should be provided until signs and symptoms have abated, stabilized, or until abnormal laboratory findings have returned to acceptable or pre-study limits. The final status of AE will be reported in the participant's study records.

Reasons for study product(s) discontinuation/withdrawal from the study should be classified as follows:

- Death.
- Adverse side effects; related or unrelated to study product(s).
- The Investigator may discontinue a participant if, in his/her judgement, it is in the best interest of the participant to do so.
- Noncompliance: defined as missing a scheduled visit by more than 2 weeks without contact.
- Participant voluntary withdrawal. A participant may withdrawal from the study at any time, for any reason.

13 RISKS TO SUBJECTS

The potential risks to participants in the clinical studies, and their likelihood and seriousness, aredescribed below

- Nicotine overdose: Some people who use nicotine products may experience symptoms of nicotine overdose such as nausea, sleep disturbance, headache, and vomiting; however, these symptoms are usually mild and temporary. Before nicotine products are used in human participants, they have undergone laboratory testing to assess the yields of nicotine present in the products; this will also provide quality control information to select the safest product.
    - The studies using nicotine products in participants will be performed in a clinical setting accustomed to monitoring for adverse events. The Principal Investigator and Co-Investigators have considerable experience with conducting outpatient studies

on novel nicotine delivery devices and their effects on participants and will be able to provide appropriate safety monitoring.

- Participants will be instructed that the investigational products are not to be ingested. If a product is ingested by mistake, the participants will be instructed to call the study physician (716-845-5412). If they are experiencing serious symptoms of nicotine overdose, the participant should contact Poison Control or Emergency Medical Services.

- Nicotine withdrawal: Many individuals who quit smoking exhibit a pattern of symptoms related to withdrawal from tobacco use. These symptoms include: sadness and anxiety, irritability, anger, difficulty concentrating, appetite change and weight gain, insomnia, and decreased heart rate. Because participants in the studies will be asked to refrain from smoking overnight, it is likely that they will experience some of these symptoms. Consent forms will include sections describing the possibility of this occurrence. Study personnel will be trained to recognize these symptoms and educate the participants about them.
- Respiratory irritation: Some people who use ENDS (Electronic Nicotine Delivery Systems) may experience irritation of the mucosal membranes of the upper respiratory tract, but this may not be likely as they are already cigarette smokers. We will exclude participants or postpone procedures if they demonstrate chronic or acute respiratory problems.
- Inconvenience: It is possible that participants will experience inconvenience due to multiple study visits required.
- Emotional distress: Participants may experience psychological discomfort during assessments when discussing feelings and attitudes about smoking and using nicotine products, or from learning about the risks of smoking. However, all participants will be current smokers and we do not expect this type of reaction to be likely. Study personnel will be alerted to expect this from a small number of participants and will be trained to make referrals for mental health services as needed. Personnel will be trained to query for adverse emotional reactions during assessments and will be trained to deal with such reactions and to provide additional referrals if needed. In addition, if assessments indicate psychiatric concerns, referrals to appropriate psychological services will be provided.
- Reproductive Risks: Women will be advised to notify the study staff if they become or intend to become pregnant during the study period. Because nicotine and ENDS vapor safety for an unborn baby is unknown, participants will be told that they should not become pregnant while on this study nor should they nurse a baby. If a woman is pregnant or breastfeeding, she may not participate in this study, and if she becomes pregnant during the study, she will be removed from the study.

As general measures to minimize the likelihood of participants experiencing these side effects, staff will have the study physician's cell phone number and will contact the study physician with all questions and concerns. We will also:

- Enroll participants in self-reported good general health
- Administer products of high quality.
- Monitor self-reported side effects at each study session. Participants will be informed about the potential for adverse events or side effects, including respiratory/oral irritation, cough,

phlegm, headache, nausea, and emotional distress from learning about the adverse health consequences of smoking. Participants will be told that they should proceed with caution until they are certain that the study products do not affect their performance.

- The study physician will be alerted to any severe side effects or any reported adverse events. The study physician will review the information provided by the research staff and if applicable, will contact the study participant within 24 hours of being notified to gather more information and determine the appropriate course of action for the participant. Ultimately, the study physician will decide if the adverse event is related to study treatment and whether the participant should discontinue its use.

Participants will be told that they should proceed with caution when using study products and to report any adverse symptoms or side effects to study personnel immediately.

14 POTENTIAL BENEFITS TO SUBJECTS

There is no direct benefit for those who decide to participate and enroll in this study.

15 DATA AND SPECIMEN BANKING

Samples Collected at Roswell Park:

All samples will be immediately transported to the Health Behavior Department Laboratory (Roswell Park Comprehensive Cancer Center). Saliva samples will be centrifuged for 2 minutes prior to storage. All samples will immediately be frozen at -20ºC or below in Dr. Goniewicz's Laboratory until analyzed (unless otherwise noted above). Female urine samples will be tested for pregnancy. All sample results are recorded in logs and kept in:

Dr. Goniewicz's Laboratory
Gratwick Basic Science Building (GBSB)
Health Behavior Department Laboratory
Laboratory location: 4th Floor, Room 4942
Laboratory phone: 716-845-8603
Dr. Goniewicz's office number: 716-845-8541

If there are remaining samples after all analysis has been done and the participant checks "YES" on the consent document to having any extra samples stored for future studies, then the samples will be kept in a -20ºC or below freezer in Dr. Maciej Goniewicz's Laboratory listed above. If there are remaining samples and the participant checks "NO" on the consent document to having any extra samples stored, then the extra samples of that participant will be immediately destroyed once they are taken off study or analyses are completed. Any future research on the remaining samples will only be done under IRB approved protocols.

EXTERNAL SITES: Follow directions above for sample collection and processing. The cryogenic tubes will be labeled with the participant identification number (Participant ID, PID) (unique to external-site participants), initials, the participant's study number, clinical study number, protocol time point, and protocol day. The saliva samples will immediately be refrigerated or frozen at -20ºC or below (samples are to be stored until requested for batch mailing).

Frozen samples will be shipped via Fed Express Overnight on dry ice with delivery on Mon-Fri. NO SATURDAY DELIVERY. Do not ship on a Friday or the day before a holiday.

Address shipments and any questions regarding specimen processing to: Maciej.Goniewicz@RoswellPark.org, telephone number: 716-845-8541.

Note: All investigator or analyzing research laboratories housing research samples need to maintain current **Temperature Logs** and study-specific **Sample Tracking and Shipping Logs**. The Principal Investigator/Laboratory Manager **must** ensure that the stated lab(s) have a process in place to document the receipt/processing/storage/shipping of study-related samples/specimens. This is required for both observational and interventional clinical studies collecting clinical samples.

Data Banking

For the purposes of this research, we will collect the following identifiable information: Participant name (to verify identification), date of birth (to verify age), telephone number and email address (to facilitate contact for scheduling). Identifiable information will be retained in a separate Excel file from the analytic dataset. The only link to identifiable information will be via a unique ID number.

All questionnaires are administered via REDCap, housed at RPCI or URMC. All data files will be electronic, including only the unique subject ID. At study completion, datafiles from RPCI and URMC will be combined and will be stored on the Cancer Prevention server (\\CancerPrev\CancerPrev$\HealthBehavior). Access to the folder is restricted to authorized users. Standard protocols for data encryption when using laptops and USB drives will be followed.

Any clinical data that is associated with the samples, will be stored on a secure server in the Department of Health Behavior, will be accessible only by the PI, Co-Investigators and PI designated data manager and, will be password protected. All computer entry and networking programs will be done using PIDs only. Any clinical data and/or specimens for future research will require verification of an IRB-approved protocol and will be de-identified before being released.

Note: All investigator or analyzing research laboratories housing research samples need to maintain current Temperature Logs and study-specific Sample Tracking and Shipping Logs. The Principal Investigator/Laboratory Manager must ensure that the stated lab(s) have a process in place to document the receipt/processing/storage/shipping of study-related samples/specimens. This is required for both observational and interventional clinical studies collecting clinical samples.

16 MEASUREMENT OF EFFECT

Nicotine boost will be measured as the post-bout saliva nicotine concentration minus the pre-bout saliva nicotine concentration.

Subjective questionnaires are scored on a 0-100 visual analog scale (some exceptions, such as -100 to 100) or a Likert scale (varying amount of points). Subjective responses will be evaluated based on their change from pre- to post-bout and for differences between products.

17 SAFETY EVALUATION

17.1 Safety Monitoring

Subjects will be monitored for safety during product use sessions by trained laboratory staff. Participants are able to use the study products ad lib and can stop product use at any time without being withdrawn from the study completely. Subjects will be given phone numbers for research associates and supervising physicians to call if there are adverse effects or other study-related problems. Subjects will be advised that if they have any adverse effects and/ or wish to stop participating in the study for any reason, they are free to do so.

The data collected from this study will be organized by a unique identification number assigned to the participant so that their identity will be available only to project staff and will remain completely confidential. The clinical study coordinator and staff and PI of the study will have access to the data records. All study records will be kept electronically in Roswell Park Comprehensive Cancer Center maintained and secured equipment. Any data, specimens, forms, reports, and other records that leave the site will be identified only by a participant identification number (Participant ID, PID) to maintain confidentiality. All records will be kept in a limited access environment. All computer entry and networking programs will be done using PIDs only. Information will not be released without written authorization of the participant.

17.2 Unanticipated problems

An Unanticipated Problem (UP) is any incident, experience, or outcome that meets all of the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given:
    - The research procedures that are described in the study-related documents, including study deviations, as well as issues related to compromise of participant privacy or confidentiality of data.
    - The characteristics of the participant population being studied.
- Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized or if in relation to an AE is deemed Serious.

17.3 Reporting Unanticipated Problems

The Reportable New Information (RNI) Form will be submitted to the CRS Quality Assurance (QA) Office within 1 business day of becoming aware of the Unanticipated Problem. After review, CRS QA Office will submit the RNI to the IRB.

When becoming aware of new information about an Unanticipated Problem, submit the updated information to CRS QA Office with an updated Reportable New Information Form. The site Investigator or designated research personnel will report all unanticipated problems to the IRB in accordance with their local institutional guidelines.

18 DATA MANAGEMENT AND CONFIDENTIALITY

To ensure data security and confidentiality, all assessments will be administered by trained research study staff. Data management activities will be performed using REDCap (Research Electronic Data Capture). REDCap is a secure web-based application that supports data capture and management for research studies. In the event of REDCap being inaccessible for a study visit, paper copies of the questionnaires will be administered to the participant at that point in time and data entry will be performed by the assigned Senior Research Associate after the study session is completed. Data can be entered and changed only by those with the rights to do so. All participant records and data will be held in the Health Behavior Department at Roswell Park Comprehensive Cancer Center. All personnel involved in the conduct of this study are Roswell Park staff.

- Access to the data by all necessary research personnel will be through a password protected network computer. At no time will data be downloaded on a thumb drive or other portable media or laptop.
- Participant identity will not be disclosed in the event of publication or sharing of data.
- Any paper files containing identifiers (if applicable to the research) will not be taken off Roswell Park premises; they will be kept in a locked filing cabinet in a secure building on the Roswell Park campus.
- PHI will not be re-used or disclosed for purposes other than research use.
- PHI (limited data set) may be shared with the partner site (URMC) to facilitate study recruitment and data analysis.
- Essential documents will be retained per Roswell Park's policy for 6 years from the study termination date. These documents could be retained for a longer period, however, If required by the applicable local regulatory requirements or by an agreement with Roswell Park.

18.1 Data Collection

Data management activities are performed using REDCap.

18.2 Maintenance of Study Documents

Essential documents will be retained per Roswell Park's policy for 6 years from the study termination date. These documents could be retained for a longer period, however, if required by the applicable local regulatory requirements or by an agreement with Roswell Park.

18.3 Revisions to the Protocol

Roswell Park may make such changes to the protocol as it deems necessary for safety reasons or as may be required by the U.S. FDA or other regulatory agencies. Revisions will be submitted to the IRB/ERC for written approval before implementation.

18.4 Termination of the Study

It is agreed that, for reasonable cause, either the Roswell Park Investigators or the Sponsor, may terminate this study, provided a written notice is submitted within the time period provided for in the Clinical Trial Agreement. In addition, Roswell Park may terminate the study at any time upon

immediate notice if it believes termination is necessary for the safety of participants enrolled in the study.

19 STATISTICAL PLAN

This is an open-label, factorial-design, multi-center study of e-liquid composition and effects on vaping topography.

19.1 Sample Size Determination

The planned sample size is n=72 evaluable patient, who are expected to complete 7 potential sessions, for a total of 504 observations.
However, we anticipate an attrition rate of 5-10% per session and the table below provides expected sample sizes under differing rates of attrition:

Session		*1*	*2*	*3*	*4*	*5*	*6*	*7*
Subjects Completed	5% Attrition	72	68	65	62	59	56	53
	10% Attrition	72	65	58	52	47	43	38
	5% 1-3 and 10% in 4-7	72	68	65	58	53	47	43

A conservative sample size calculation is based on comparing any two flavors or nicotine formulations using a two-sided paired t-test. The minimum expected sample size per combination is expected to be between 38 and 53; which provides 80% power (at α=0.05) to detect a difference of at least 0.47 and 0.39 standard deviations. Since the actual models used in the analysis will account for additional sources of variability and will borrow information across sessions, the actual detectable effect sizes may be larger.

19.2 Randomization

Subjects will complete up to 7 sessions. At each session, subjects will complete directed and ad lib bouts of vaping. The order of directed and ad lib bouts will be randomized within participant using a permutation block design (block sizes of 2 and 4).

Session 1 will use their own-brand liquid. No randomization is required.

Sessions 2-5 will evaluate the relationship of tobacco flavor formulation (no flavor and 3 commercial flavor variants) on outcomes. The order of nicotine forms (i.e., what flavor is experienced at a given session) will be randomized using a permuted Latin Square design.

Sessions 6-7 will evaluate the relationship of nicotine formulation (2 forms) on outcomes. The order of nicotine forms will be randomized using a permuted Latin Square design.

19.3 Demographics and Baseline Characteristics

Descriptive statistics (as appropriate: n, percent, mean, median, min and max) will be used to summarize demographic and baseline characteristics.

19.4 Primary Analysis

The primary objective is to evaluate the influence of:

a. tobacco flavoring composition on vaping topography

b. synthetic vs. tobacco derived nicotine on vaping topography

The primary endpoints are measures of vaping topography, which are treated as quantitative outcomes and will be summarized by condition (flavor or nicotine composition) and bout (directed or ad-lib) using the appropriate descriptive statistics.

Using data from sessions 1-5, each endpoint will be modeled as a function of flavoring (own, none, and 3 commercial flavors), bout (directed or ad-lib), their two-way interaction, and random subject and site effects using a linear mixed model. Tests about the appropriate contrasts of model estimates will be used to compare:

i) mean differences between flavors within a type of bout,
ii) mean differences between bouts within a flavor,
iii) effects of bout (ad lib – directed) between flavors,
iv) effect of flavor between bouts.

Using data from sessions 6 & 7, each endpoint will be modeled as a function of nicotine composition (synthetic vs. tobacco derived), bout (directed or ad-lib), their two-way interaction, and random subject and site effects using a linear mixed model. Tests about the appropriate contrasts of model estimates will be used to compare:

i) mean differences between composition within a type of bout,

ii) mean differences between bouts within a composition,

iii) effects of bout (ad lib – directed) between compositions,

iv) effect of composition between bouts.

19.5 Secondary Analysis

The models described above will be used to evaluate the effect of flavoring and nicotine formulation on sensory measures.

20 PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF SUBJECTS

Subjects will be monitored for safety during product use sessions by trained laboratory staff. Participants are able to use the study products ad lib and can stop product use at any time without being withdrawn from the study completely. Subjects will be given phone numbers for research associates and supervising physicians to call if there are adverse effects or other study-related problems. Subjects will be advised that if they have any adverse effects and/ or wish to stop participating in the study for any reason, they are free to do so.

The data collected from this study will be organized by a unique identification number assigned to the participant so that their identity will be available only to project staff and will remain completely confidential. The clinical study coordinator, study staff, and PI of the study will have access to the data records. All study records will be kept electronically in Roswell Park Comprehensive Cancer Center maintained and secured equipment. Any data, specimens, forms, reports, and other records that leave the site will be identified only by a participant identification number (Participant ID, PID) to maintain confidentiality. All records will be kept in a limited

access environment. All computer entry and networking programs will be done using PIDs only. Information will not be released without written authorization of the participant.

21 VULNERABLE POPULATIONS

N/A

22 COMMUNITY-BASED PARTICIPATORY RESEARCH

N/A

23 SHARING OF RESULTS WITH SUBJECTS

Positive pregnancy test results will be shared with participants where applicable.

24 SETTING

All study sessions will take place in The Health Behavior Human Exposure Lab located at Roswell Park Comprehensive Cancer Center or an equivalent laboratory environment at the University of Rochester Medical Center (URMC). The research team will identify and recruit potential participants from the Western New York region.

25 PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF SUBJECTS

Any data, specimens, forms, reports, video recordings, and other records that leave the site will be identified only by a participant identification number (Participant ID, PID) to maintain confidentiality. All records will be kept in a limited access environment. All computer entry and networking programs will be done using PIDs only. Information will not be released without written authorization of the participant.

26 RESOURCES AVAILABLE

Investigators on this protocol have the education and research training and experience to conduct this study safely and appropriately. All data and specimen collection will be done by trained clinical research coordinators, research associates or certified phlebotomists working on this study.

All study procedures at RPCI will be performed in the:

Health Behavior Human Exposure Lab
Gratwick Basic Science Building (GBSB)
Laboratory location: 3rd Floor, Room 3920
Laboratory phone: 716-845-3312

The laboratory is 10’ x 10.5” x 11’8” space equipped with a sink, multiple infusion chairs, and an Axis Communications video camera. In addition, the laboratory also has specialized mechanical exhausts and ducts designed to keep the room under negative air pressure at all times.

University of Rochester Medical Center (URMC) will be an additional study site. The site PI is Dr. Deborah Ossip. A reliance agreement will be entered wherein Roswell Park is the IRB of record.

Dr. Nicholas Felicione (SUNY Buffalo) will be providing technical assistance on topography device use, troubleshooting, and interpretation. Dr. Felicione will be acting primarily in an advisory capacity and will not have access to any data containing PHI.

27 PRIOR APPROVALS

Not applicable.

28 COMPENSATION FOR RESEARCH-RELATED INJURY

If the subject believes they have been injured as a direct result of their participation in this research study, they will be advised to notify the Roswell Park Patient Advocate at (716) 845-1365 or the Study Doctor at (716) 845-4517.

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

The subject is not prevented from seeking to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research.

29 ECONOMIC BURDEN TO SUBJECTS

Participants will be responsible for transportation to and from the research site and any costs that might entail. The remainder of the study will be conducted at no financial cost or obligation to the participant.

30 CONSENT PROCESS

The Roswell Park SOP: Informed Consent Process for Research (HRP-090) will be followed.

Consent will be obtained at Session 1 before any tests, procedures, or questionnaires (other than eligibility screeners) are administered in the tobacco research laboratory.

Each participant shall read, understand, and sign an instrument of informed consent prior to performance of any study-specific procedure. It is the responsibility of the investigator to ensure that the participant is made aware of the investigational nature of the treatment and that informed consent is given. Consent will be obtained at the beginning at the first visit prior to any data collection. Research staff will guide participants through the consent form, provide the participant time to read the consent form, and answer any questions. Participants will verbally consent, sign the consent form (physically or electronically), and show the consent form to research staff to ensure it is filled out correctly. The research staff will sign their copy of the consent form upon verbal consent and demonstration of signing the consent form. The signed consent form (or a photograph of signed consent) will then be returned to research staff through secure email or drop off/pick up.

Consent may be obtained through the REDCap (Research Electronic Data Capture) system used for data collection. REDCap is a secure web-based application that supports data capture and management for research studies. The Investigator and Research Associate will design the study specific consent and upload the most recent CRS version to the REDCap system. A secure link will be sent to each participant prior to the start of the study. Research staff will guide the

participant form, provide time to read the consent, and answer any questions. Participants will be able to electronically sign, date, and submit the consent in real-time. Once the consent is submitted, it is automatically saved on Roswell Park protected servers.

In the event of REDCap being inaccessible for a study visit, pdf files or paper copies of the consent will be administered, and the participant will be able to either sign and return or submit a photo of the signed copy as stated above.

All RedCap consent files will be stored on protected servers at Roswell Park. Access to this folder is restricted to authorized users. Standard protocols for data encryption when using laptops and USB drives will be followed.

The Investigator is responsible for the retention of the participant log and participant records; although personal information may be reviewed by authorized persons, that information will be treated as strictly confidential and will not be made publicly available. The investigator is also responsible for obtaining participant authorization to access medical records and other applicable study specific information according to Health Insurance Portability and Accountability Act regulations (where applicable).

This study will be conducted in compliance with all applicable laws and regulations of the state and/or country and institution where the participant is treated. The clinical trial should be conducted in accordance with the ethical principles embodied in the Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, consistent with good clinical practice and the applicable regulatory requirements and according to the guidelines in this protocol, including attached appendices.

31 PROCESS TO DOCUMENT CONSENT IN WRITING

The Roswell Park SOP: Written Documentation of Consent (HRP-091) will be followed.

Consent will be obtained at Session 1 before any tests, procedures, or questionnaires (other than eligibility screeners) are administered in the tobacco research laboratory.

The Investigator (or IRB specified designee) is responsible for obtaining written consent from each participant in accordance with GCP guidelines using the approved informed consent form, before any study specific procedures (including screening procedures) are performed. The informed consent form acknowledges all information that must be given to the participant according to applicable GCP guidelines, including the purpose and nature of the study, the expected efficacy and possible side effects of the s(s), and specifying that refusal to participate will not influence further options for therapy. Any additional information that is applicable to the study must also be included. Additional national or institutionally mandated requirements for informed consent must also be adhered to. The participant should also be made aware that by signing the consent form, processing of sensitive clinical trial data and transfer to other countries for further processing is allowed.

The Investigator or designee shall provide a copy of the signed consent form to the participant and the signed original shall be maintained in the Investigator File. A copy of the signed consent form must be filed in the participant file. At any stage, the participant may withdraw from the study and such a decision will not affect any further treatment options.

32 DRUGS OR DEVICES

During each visit, participants will be asked to use E-liquids (unflavored, tobacco flavor). The primary psychoactive ingredient in all products is nicotine. All products are currently available for commercial purchase and will be purchased by the research team either online or at local stores (e.g., tobacco/vape shops, convenience store). These nicotine-containing products will be stored in a cool, dark location in laboratories or offices that are locked and only accessible to those with a key. When participants are randomized to a condition, the laboratory staff session will retrieve only the product needed for the individual session and will bring it directly to the participant in the lab.

Under no circumstances will the Investigator allow the study product to be used in a manner other than as directed by this protocol.

33 REFERENCES

1. Carpenter CM, Wayne GF, Connolly GN. The role of sensory perception in the development and targeting of tobacco products. Addiction. 2007;102(1):136-47. doi: 10.1111/j.1360-0443.2006.01649.x. PubMed PMID: 17207131.

2. Kreslake JM, Wayne GF, Connolly GN. The menthol smoker: tobacco industry research on consumer sensory perception of menthol cigarettes and its role in smoking behavior. Nicotine Tob Res. 2008;10(4):705-15. doi: 10.1080/14622200801979134. PubMed PMID: 18418792.

3. Kreslake JM, Yerger VB. Tobacco industry knowledge of the role of menthol in chemosensory perception of tobacco smoke. Nicotine Tob Res. 2010;12 Suppl 2:S98-101. Epub 2011/01/05. doi: 10.1093/ntr/ntq208. PubMed PMID: 21177374.

4. Megerdichian CL, Rees VW, Wayne GF, Connolly GN. Internal tobacco industry research on olfactory and trigeminal nerve response to nicotine and other smoke components. Nicotine Tob Res. 2007;9(11):1119-29. doi: 10.1080/14622200701648458. PubMed PMID: 17978985.

5. Rees VW, Kreslake JM, Cummings KM, O'Connor RJ, Hatsukami DK, Parascandola M, Shields PG, Connolly GN. Assessing consumer responses to potential reduced-exposure tobacco products: a review of tobacco industry and independent research methods. Cancer Epidemiol Biomarkers Prev. 2009;18(12):3225-40. doi: 10.1158/1055-9965.EPI-09-0946. PubMed PMID: 19959675; PMCID: PMC2790162.

6. Rose JE, Tashkin DP, Ertle A, Zinser MC, Lafer R. Sensory blockade of smoking satisfaction. Pharmacology, biochemistry, and behavior. 1985;23(2):289-93. Epub 1985/08/01. PubMed PMID: 4059314.

7. Rose JE, Zinser MC, Tashkin DP, Newcomb R, Ertle A. Subjective response to cigarette smoking following airway anesthetization. Addictive behaviors. 1984;9(2):211-5. Epub 1984/01/01. PubMed PMID: 6741683.

8. Rose JE. Nicotine and nonnicotine factors in cigarette addiction. Psychopharmacology. 2006;184(3-4):274-85. Epub 2005/12/20. doi: 10.1007/s00213-005-0250-x. PubMed PMID: 16362402.

9. Rose JE, Behm FM. Extinguishing the rewarding value of smoke cues: pharmacological and behavioral treatments. Nicotine Tob Res. 2004;6(3):523-32. Epub 2004/06/19. doi: 10.1080/14622200410001696501. PubMed PMID: 15203786.

10. Rose JE, Behm FM, Levin ED. Role of nicotine dose and sensory cues in the regulation of smoke intake. Pharmacology, biochemistry, and behavior. 1993;44(4):891-900. Epub 1993/04/01. PubMed PMID: 8469698.

11. Rose JE, Behm FM, Westman EC, Bates JE, Salley A. Pharmacologic and sensorimotor components of satiation in cigarette smoking. Pharmacology, biochemistry, and behavior. 2003;76(2):243-50. Epub 2003/11/01. PubMed PMID: 14592675.

12. Rose JE, Behm FM, Westman EC, Johnson M. Dissociating nicotine and nonnicotine components of cigarette smoking. Pharmacology, biochemistry, and behavior. 2000;67(1):71-81. Epub 2000/12/13. PubMed PMID: 11113486.

13. Westman EC, Behm FM, Rose JE. Airway sensory replacement combined with nicotine replacement for smoking cessation. A randomized, placebo-controlled trial using a citric acid inhaler. Chest. 1995;107(5):1358-64. Epub 1995/05/01. PubMed PMID: 7750331.

14. Westman EC, Behm FM, Rose JE. Dissociating the nicotine and airway sensory effects of smoking. Pharmacology, biochemistry, and behavior. 1996;53(2):309-15. Epub 1996/02/01. PubMed PMID: 8808137.

15. Ashare RL, Hawk LW, Jr., Cummings KM, O'Connor RJ, Fix BV, Schmidt WC. Smoking expectancies for flavored and non-flavored cigarettes among college students. Addictive behaviors. 2007;32(6):1252-61. Epub 2006/10/13. doi: 10.1016/j.addbeh.2006.08.011. PubMed PMID: 17030447.

16. Hanson K, O'Connor R, Hatsukami D. Measures for assessing subjective effects of potential reduced-exposure products. Cancer Epidemiol Biomarkers Prev. 2009;18(12):3209-24. doi: 10.1158/1055-9965.EPI-09-0971. PubMed PMID: 19959674; PMCID: PMC2821025.

17. Harrell PT, Juliano LM. A direct test of the influence of nicotine response expectancies on the subjective and cognitive effects of smoking. Experimental and clinical psychopharmacology. 2012;20(4):278-86. Epub 2012/06/20. doi: 10.1037/a0028652. PubMed PMID: 22708609.

18. Hendricks PS, Brandon TH. Smoking expectancy associates among college smokers. Addictive behaviors. 2005;30(2):235-45. doi: 10.1016/j.addbeh.2004.05.006. PubMed PMID: 15621395.

19. Hendricks PS, Brandon TH. Smokers' expectancies for smoking versus nicotine. Psychol Addict Behav. 2008;22(1):135-40. doi: 10.1037/0893-164X.22.1.135. PubMed PMID: 18298240.

20. O'Connor RJ, Ashare RL, Fix BV, Hawk LW, Cummings KM, Schmidt WC. College students' expectancies for light cigarettes and potential reduced exposure products. American journal of health behavior. 2007;31(4):402-10. doi: 10.5555/ajhb.2007.31.4.402. PubMed PMID: 17511575.

21. Wetter DW, Smith SS, Kenford SL, Jorenby DE, Fiore MC, Hurt RD, Offord KP, Baker TB. Smoking outcome expectancies: factor structure, predictive validity, and discriminant validity. J Abnorm Psychol. 1994;103(4):801-11. PubMed PMID: 7822583.

22. Hiler M, Karaoghlanian N, Talih S, Maloney S, Breland A, Shihadeh A, Eissenberg T. Effects of electronic cigarette heating coil resistance and liquid nicotine concentration on user nicotine delivery, heart rate, subjective effects, puff topography, and liquid consumption. Experimental and clinical psychopharmacology. 2020;28(5):527-39. Epub 2019/12/20. doi: 10.1037/pha0000337. PubMed PMID: 31855003; PMCID: PMC9159736.

23. Spindle TR, Talih S, Hiler MM, Karaoghlanian N, Halquist MS, Breland AB, Shihadeh A, Eissenberg T. Effects of electronic cigarette liquid solvents propylene glycol and vegetable glycerin on user nicotine delivery, heart rate, subjective effects, and puff topography. Drug Alcohol Depend. 2018;188:193-9. Epub 2018/05/21. doi: 10.1016/j.drugalcdep.2018.03.042. PubMed PMID: 29778773; PMCID: PMC7193252.

24. Kimber CF, Soar K, Dawkins LE. Changes in puffing topography and subjective effects over a 2-week period in e-cigarette naïve smokers: Effects of device type and nicotine concentrations. Addictive behaviors. 2021;118:106909. doi: https://doi.org/10.1016/j.addbeh.2021.106909.

25. Talih S, Salman R, Karaoghlanian N, El-Hellani A, Saliba N, Eissenberg T, Shihadeh A. "Juice Monsters": Sub-Ohm Vaping and Toxic Volatile Aldehyde Emissions. Chemical Research in Toxicology. 2017;30(10):1791-3. doi: 10.1021/acs.chemrestox.7b00212.

26. Son Y, Weisel C, Wackowski O, Schwander S, Delnevo C, Meng Q. The Impact of Device Settings, Use Patterns, and Flavorings on Carbonyl Emissions from Electronic Cigarettes. Int J Environ Res Public Health. 2020;17(16). Epub 2020/08/09. doi: 10.3390/ijerph17165650. PubMed PMID: 32764435; PMCID: PMC7460324.

27. Bartoshuk LM. Comparing sensory experiences across individuals: recent psychophysical advances illuminate genetic variation in taste perception. Chem Senses. 2000;25(4):447-60. PubMed PMID: 10944509.

28. Felicione NJ, Karaoghlanian N, Shihadeh A, Eissenberg T, Blank MD. Comparison of Measurement Methods for Electronic Cigarette Puff Topography. Tob Regul Sci. 2020;6(5):318-30. Epub 2021/05/08. doi: 10.18001/trs.6.5.2. PubMed PMID: 33959673; PMCID: PMC8096180.

29. Mazur JE. An adjusting procedure for studying delayed reinforcement. In: M.L. Commons JEM, J.A. Nevin, H. Rachlin, editor. Qantitative Analysis of Behavior. Hillsdale, NJ: Erlbaum; 1987. p. 55-73.

34 APPENDICES/ SUPPLEMENTS

Appendix A Recruitment Materials (Print Ad Copy)

ROSWELL PARK®
COMPREHENSIVE CANCER CENTER

RESEARCH PARTICIPANTS
NEEDED

Researchers at Roswell Park are searching for **current daily vapers to participate in a laboratory research study**.

Participation involves up to 7 sessions that last about 1 hour each.

Must be 21+ years old daily vaper to participate.

Participants will be compensated
for their time.

If interested, please contact [716-845-3456 or CROFT@roswellpark.org and ask for the TOPOG study

Appendix B Study Screeners

Appendix B1: Core Eligibility Screener

Core Eligibility Screener

Name: _____

Preferred Phone Number_____
Type of phone: _____ Land Line ____ Mobile
If Mobile Phone, may we text you? ___ yes ___no ___ only if necessary

1. Do you currently use tobacco products? By currently, we mean any use at all in the last month (30 days)
___ Yes (please proceed to question 2)
___ No (please proceed to question 3)

2. Which tobacco products have you used in the past 30 days? Please check all that apply.
___ Cigarettes
___ Cigars
___ Cigarillos
___ Clove Cigarettes
___ Herbal Cigarettes
___ Bidis
___ Pipe Tobacco
___ Roll Your Own
___ Chewing Tobacco
___ Moist Snuff
___ Snus
___ E-Cigarettes
___ Vapes
___JUUL
___Nicotine pouches (i.e.: Zyn, On!, Velo)
___Nicotine gummies
___Nicotine gum
___Nicotine lozenges
___ No products. I do not use tobacco or nicotine products.
(Please proceed to question 6)

3. Have you used tobacco or nicotine products in the past?
___ Yes (please proceed to question 4)
___ No (please proceed to question 6)

4. What products did you use? Please check all that apply.
___ Cigarettes
___ Cigars
___ Cigarillos
___ Clove Cigarettes
___ Herbal Cigarettes
___ Bidis
___ Pipe Tobacco
___ Roll Your Own
___ Chewing Tobacco
___ Moist Snuff
___ Snus
___ E-Cigarettes
___ Vapes
___JUUL
___Nicotine pouches (i.e.: Zyn, On!, Velo)
___Nicotine gummies
___Nicotine gum
___Nicotine lozenges

5. How long ago did you quit smoking?
___ More than a year ago
___ Less than a year ago
___ Less than 6 months ago
___ Less than a month ago

6. Have you used any Nicotine Replacement medication such as the patch, gum, lozenge, spray, or inhaler in the past 30 days?
___ Yes
___ No

7. Do you smoke cigarettes some days or every day?
___ Some Days
___ Every Day
___ Not at all

8. How many cigarettes do you smoke per day? Please enter a number.
_____

9. How long have you been smoking?
___ More than 1 year
___ Less than 1 year
___ Not at all

10. Have you tried to quit smoking in the past 30 days?
(more than a 24 hour time period without smoking)
___ Yes
___ No
___ Not a smoker

11. Are you seriously thinking of quitting smoking?
___ Yes, within the next 30 days
___ Yes, within the next 6 months
___ No, not thinking of quitting
___ Not a smoker

12. How would you describe your gender identity? (for demographics purposes, only)
__Male
__Female
__Trans-male
__Trans-female
__A different gender identity not listed above

13. What is your age? Please enter a number (years).
_____

14. Please describe your overall health.
___ Excellent
___ Very Good
___ Good
___ Fair
___ Poor

15. Please describe your overall mental health.
___ Excellent
___Very Good
___Good
___ Fair
___ Poor

16 MEN. How many times in the past year have you had 5 or more alcoholic drinks in a day? Please enter the number below.
_____

16 WOMEN. How many times in the past year have you had 4 or more alcoholic drinks in a day? Please enter the number below.
_____

17. Are you currently involved in any other Roswell Park research studies?
___ Yes
___ No

End Script: Thank you for completing the Roswell Park Cancer Institute, Health Behavior Core Screener. Congratulations on your preliminary eligibility! We currently have several ongoing studies and want to place you with the best one based on your eligibility.

1. Would you like to be called for study-specific eligibility?
___ Yes (please proceed to question 2)
___No, I do not wish to leave a phone number (please proceed to question 6)

2. Please enter your name.
_____

3. Please enter your phone number, starting with the area code.
___ ___ ___ - ___ ___ ___ - ___ ___ ___ ___

4. What day(s) would be the best to reach you? Please check all that apply.
___ Monday
___ Tuesday
___ Wednesday
___ Thursday
___ Friday
___ Saturday
___ Sunday

5. What time of day would be best to reach you? Please check all that apply.
___ Morning (8am – 12pm)
___ Afternoon (12pm – 4pm)
___ Evening (4pm – 8pm)

6. Would you like to be emailed for study-specific eligibility?
___ Yes (please proceed to question 7)
___ No, I do not wish to leave an email address (please proceed to question 9)

7. Please enter your name.
_____

8. Please enter your email address.
_____

9. For more information on study-specific eligibility, please call the Roswell Park Cancer Institute, CRoFT Study Line at 716-845-___ ___ ___ ___ or email CROFT@roswellpark.org. Thank you for your time and have a great day.

Appendix B2: Study Specific Eligibility Screener

Additional Study-Specific Eligibility Questions

1. Are you between 21 and 55 years old?
   a. ____Yes
   b. ____ No
2. What is your birthdate?
   __mm__/__dd___/_yyyy__
3. Do you use vapes? This includes e-cigarettes, vaporizers, and JUUL.
   a. ____Yes
   b. ____ No
4. If yes, what type?
   a. List choices
5. Do you now vape every day, some days, or not at all?
   a. ____Everyday
   b. ____Some Days
   c. ____Not at all
6. Do your vapes/e-cigarettes/JUUL contain nicotine?
   a. ____Yes
   b. ____ No
7. Are your vapes/e-cigarettes/JUUL flavored?
   a. ____Yes
   b. ____ No
8. If yes, which of the following best describes the flavor you are using now. Check all that apply.
   a. Fruit - Berry
   b. Fruit - Citrus
   c. Fruit - Tropical
   d. Fruit – Other
   e. Desserts
   f. Candy
   g. Other sweets
   h. Tobacco
   i. Menthol or mint
   j. Nuts
   k. Spices
   l. Coffee/Tea
   m. Alcoholic beverage
   n. Other beverage
   o. Something else: _____

9. Which of these products do you NOT like / be willing to use? Check all that apply
    a. Fruit - Berry
    b. Fruit - Citrus
    c. Fruit - Tropical
    d. Fruit – Other
    e. Desserts
    f. Candy
    g. Other sweets
    h. Tobacco
    i. Menthol or mint
    j. Nuts
    k. Spices
    l. Coffee/Tea
    m. Alcoholic beverage
    n. Other beverage

10. Do you use any other tobacco products daily?
    a. ____Yes
    b. ____ No

11. Do you have any intentions to quit vaping?
    a. Yes – In the next 2 weeks
    b. Yes – In the next month
    c. Yes – In the next 6 months
    d. Yes – in the next year
    e. **No intention to quit**

12. Please describe your overall health.
    ___ a. Excellent
    ___ b. Very Good
    ___ c. Good
    ___ d. Fair
    ___ e. Poor

13. Please describe your overall mental health.
    ___a. Excellent
    ___b. Very Good
    ___c. Good
    ___d. Fair
    ___ e. Poor

14. Are you able to speak, read, and write in English?
    a. ____Yes
    b. ____No

15. Are you male or female?
    a. ____Male

b. ____Female
c. ____Undetermined
d. ____Refused

16. If female, are currently pregnant?
    a. Yes
    b. No

17. Do you plan to become pregnant within the next 12 months?
    a. Yes
    b. No

18. Are you currently breastfeeding?
    a. Yes
    b. No

19. Do you have any known allergies?
    a. Yes
    b. No
20. Please list your allergies
    a. _____
    b. _____
    c. _____
    d. _____
    e. _____
21. Do you have the ability to both smell and taste?
    a. Yes
    b. No
22. Are you on any medications that might interfere with your ability to smell and taste?
    a. Yes
    b. No
23. Are you able to participate in several 1 hour sessions over the span of 3 months?
    a. Yes
    b. No
24. Do you have reliable transportation to travel to and from Roswell Park for a total of 7 sessions over the course of 3 months?

Appendix C Questionnaires

Demographics

Please answer each question directly on this questionnaire packet by writing, checking, or circling the correct answer or, where spaces are provided, writing in your answer.

1. What is your date of birth?

_____ (month) _____(date) _____(year)

2a. What sex were you assigned at birth?

Male
Female

2b. What gender do you currently identify as?
_Male
_Female
_Trans-male
_Trans-female
_A different gender identity not listed above

3. Are you Spanish, Hispanic, or Latino?

No
Yes

4. How would you describe your race?
White, Caucasian
Black, African American
American Indian or Alaska Native
Asian
Native Hawaiian or other Pacific Islander
Other _____

5. What is the highest level of school you completed or the highest degree you received?

- ❑ Never attended school
- ❑ Less than high school
- ❑ High school graduate
- ❑ G.E.D.
- ❑ Some technical or vocational school
- ❑ Some college, no degree
- ❑ AA; technical or vocational school
- ❑ BA, BS college graduate
- ❑ At least some graduate or professional school
- ❑ Graduate or professional degree
- ❑ Don’t know

6. What is your yearly average household income?

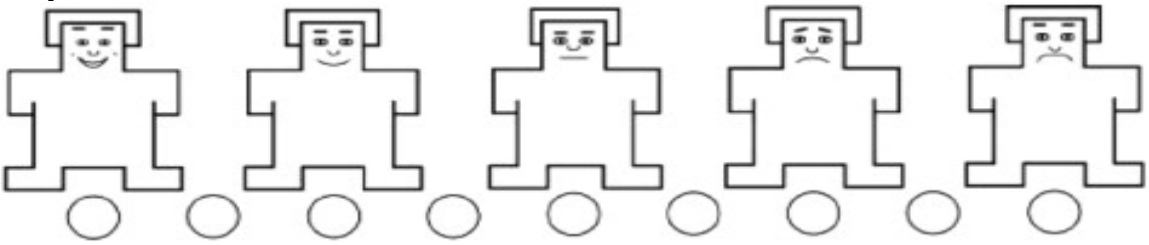
- ❑ $30,000 or less
- ❑ $30,001-$60,000
- ❑ $60,001 or more
- ❑ Prefer not to answer

Taste Preferences: Meier et al JPSP 2012

For each of the foods shown below, please check the box that corresponds to how much you like or dislike that food. If you have never tried a food, please check that box.

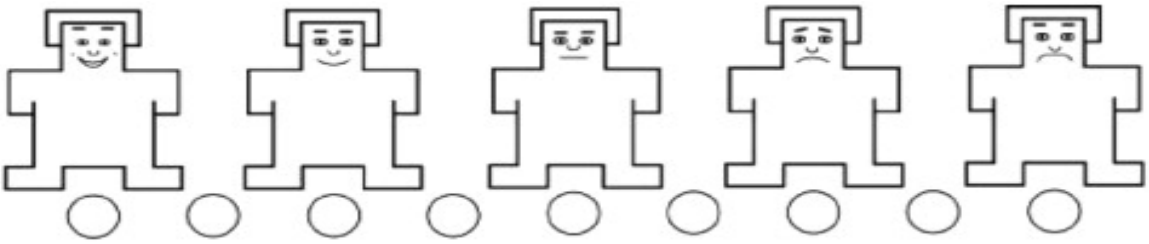
Sweet items:

Candy



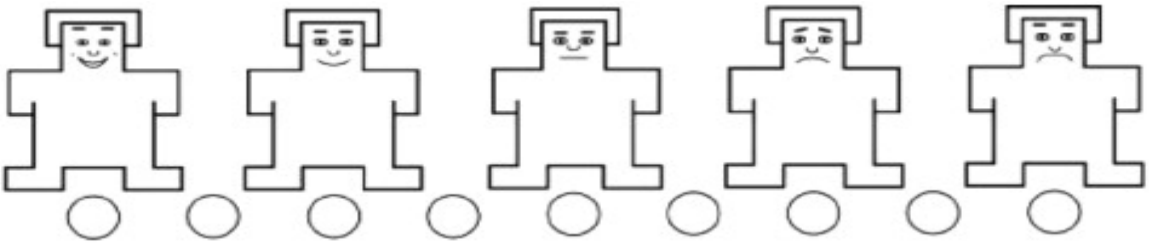
___ Never tried

Caramel



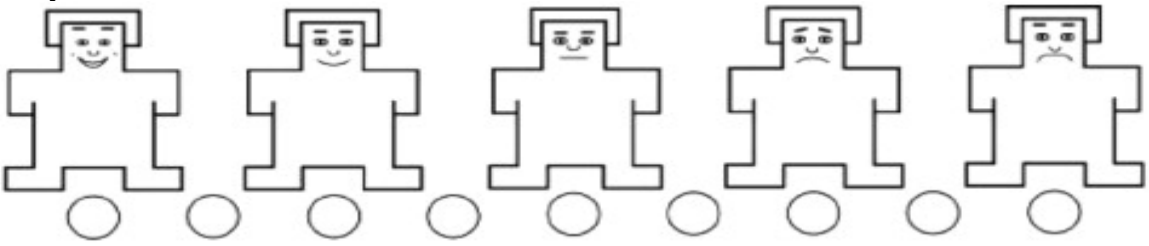
___ Never tried

Chocolate Cake



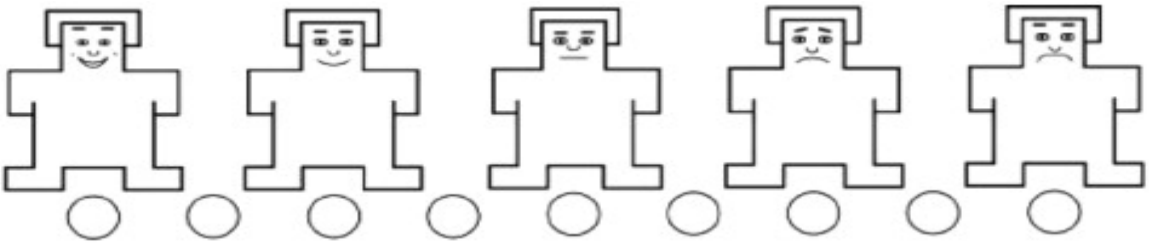
___ Never tried

Honey



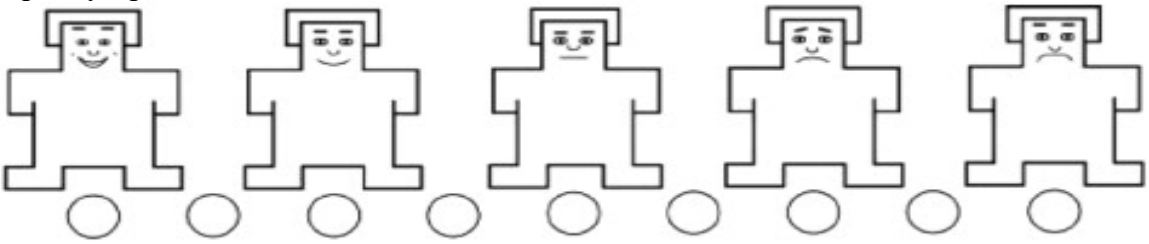
___ Never tried

Ice cream



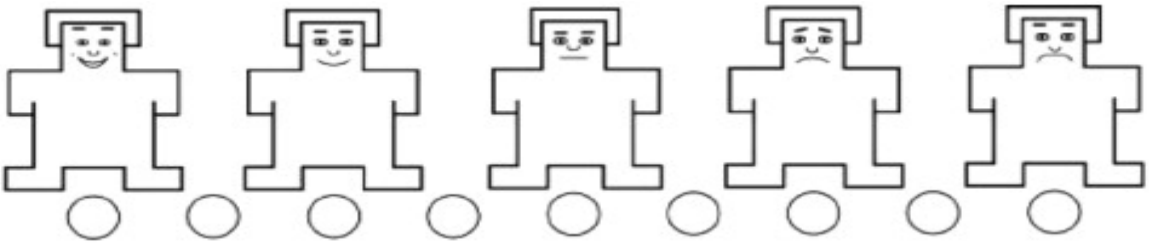
___ Never tried

Maple Syrup



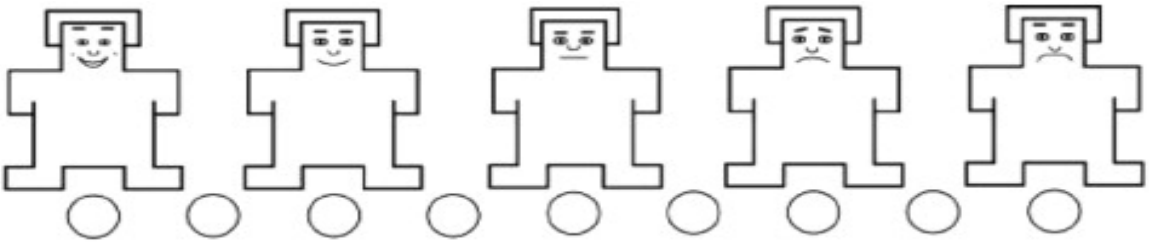
___ Never tried

Pears



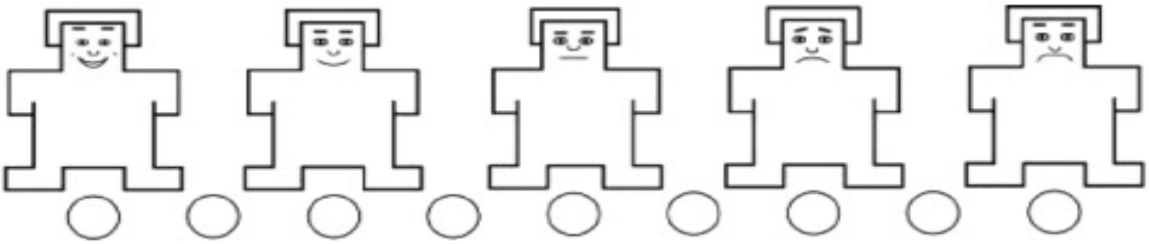
___ Never tried

Raisins



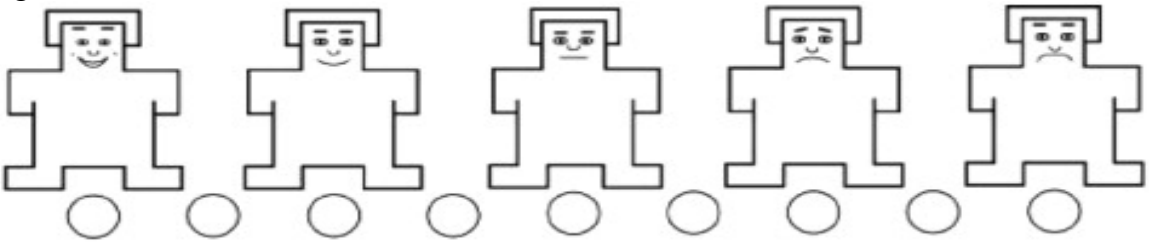
___ Never tried

Strawberries



___ Never tried

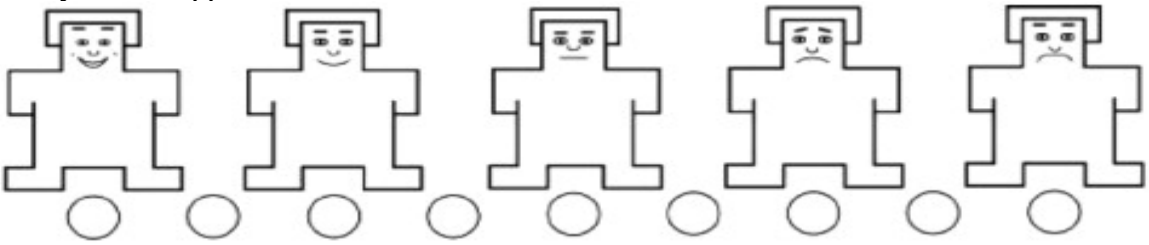
Sugar



___ Never tried

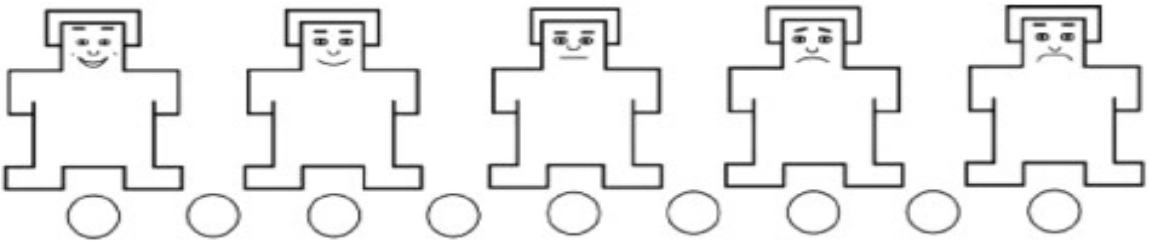
Sour items:

Granny Smith Apples



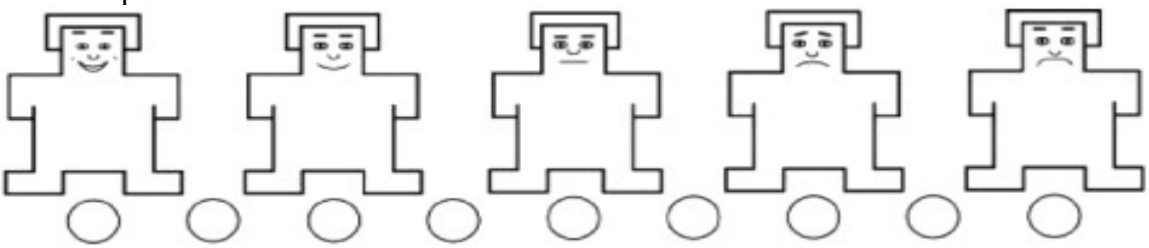
___ Never tried

Lemons



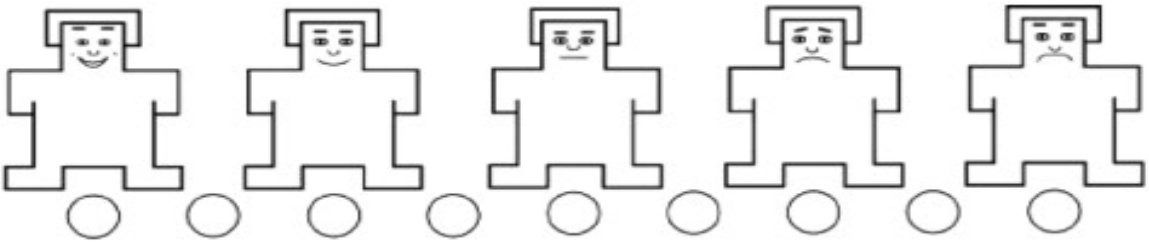
___ Never tried

Lemon drops



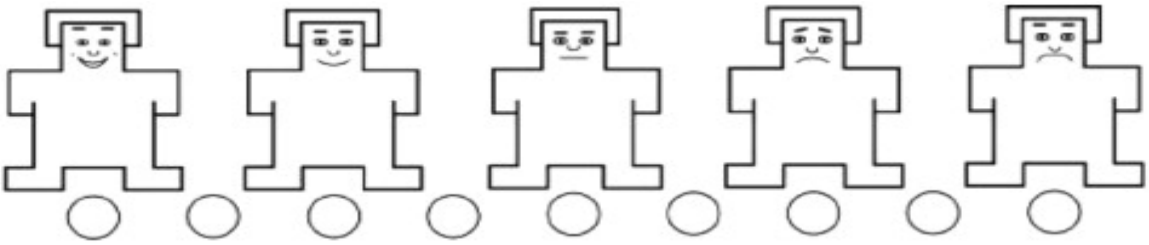
___ Never tried

Limes



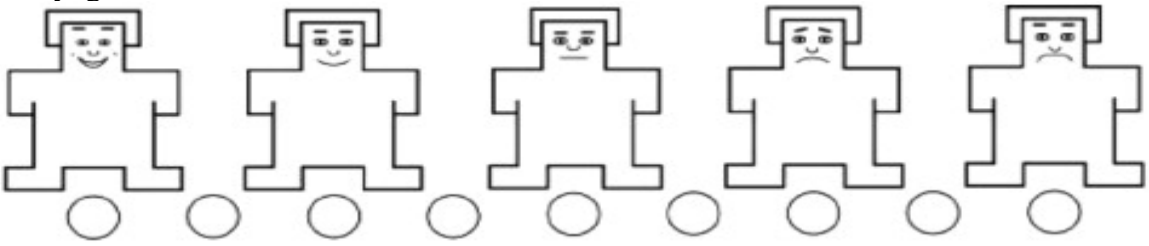
___ Never tried

Lime Sherbet



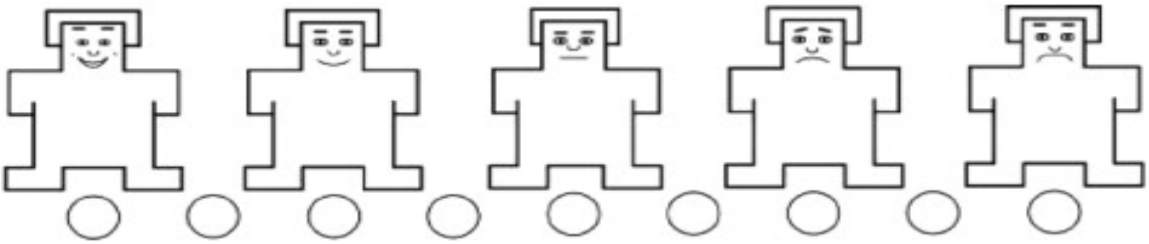
___ Never tried

Plain yogurt



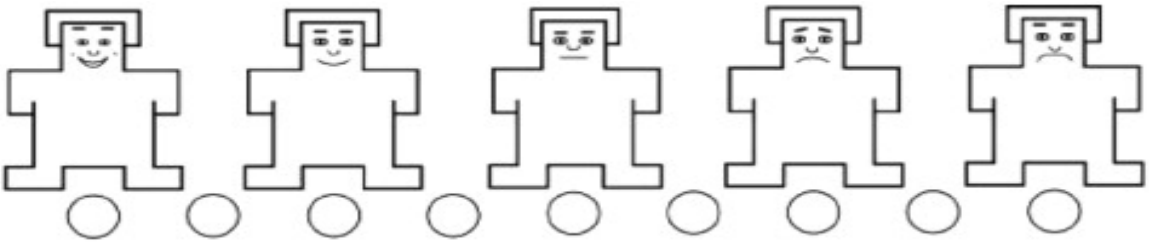
___ Never tried

Sauerkraut



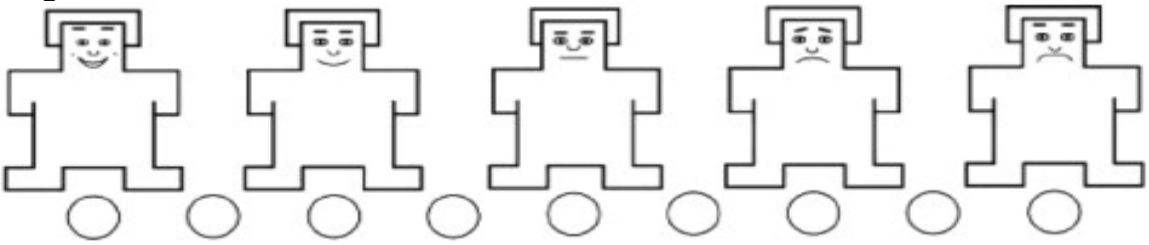
___ Never tried

Sour Cream



___ Never tried

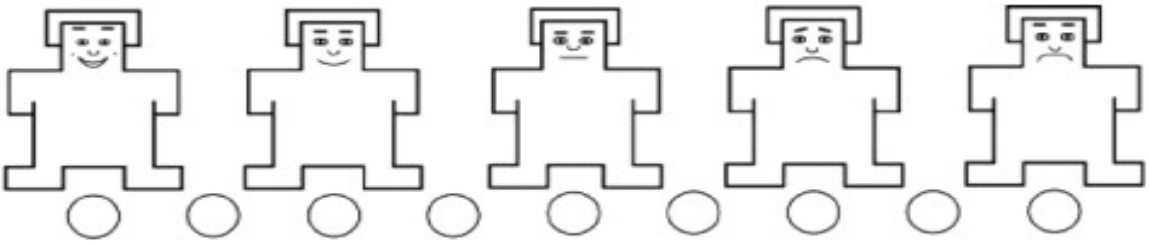
Vinegar



___ Never tried

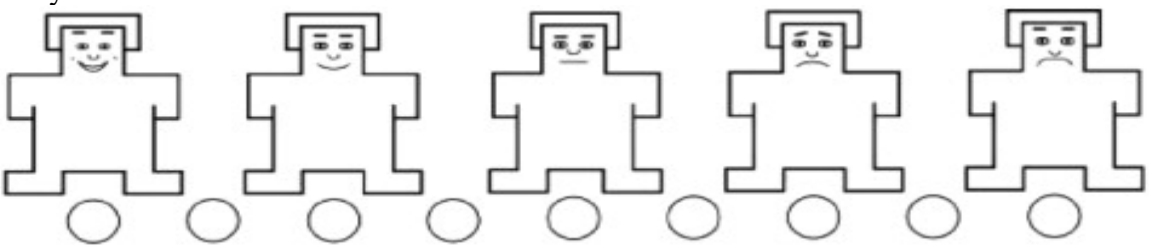
Bitter items:

Beer



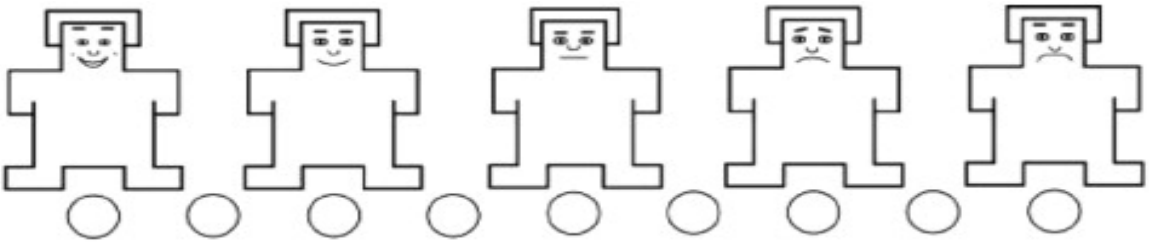
___ Never tried

Celery



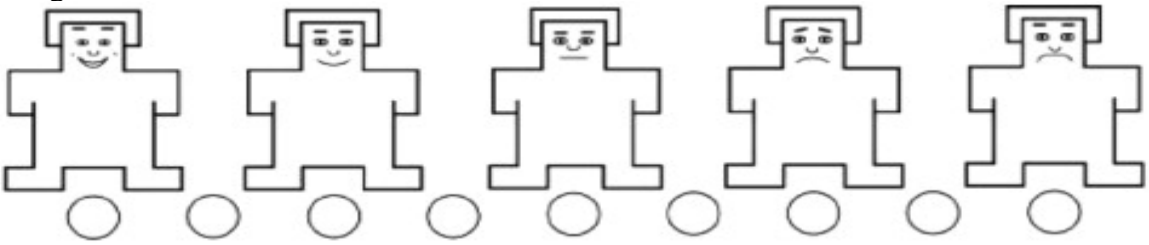
___ Never tried

Coffee



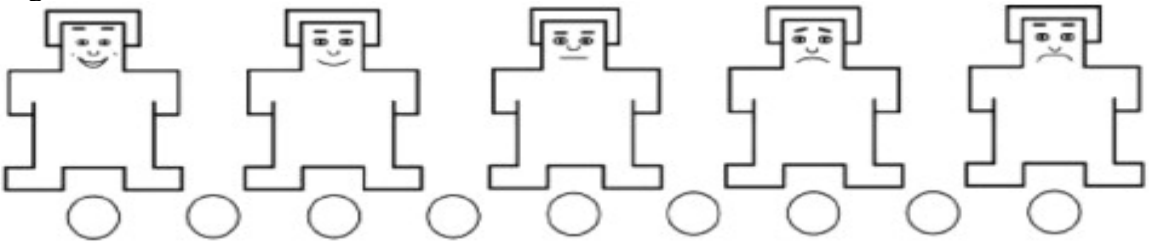
___ Never tried

Cottage cheese



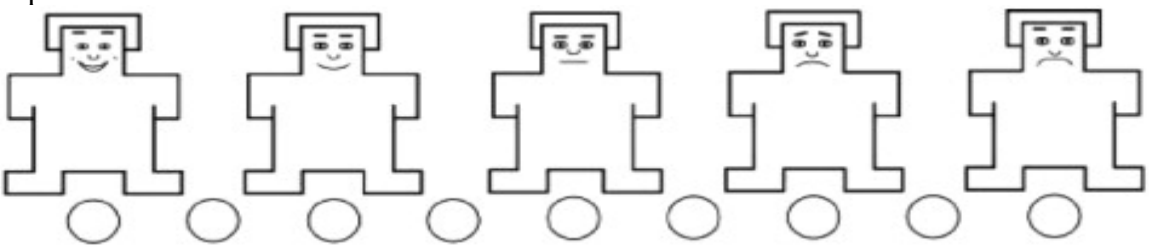
___ Never tried

Ginger Ale



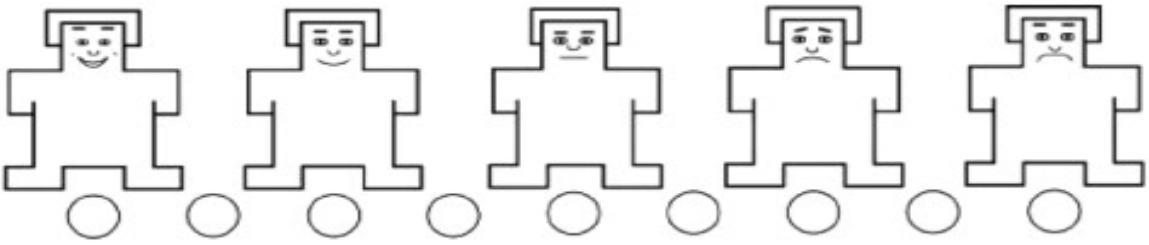
___ Never tried

Grapefruit



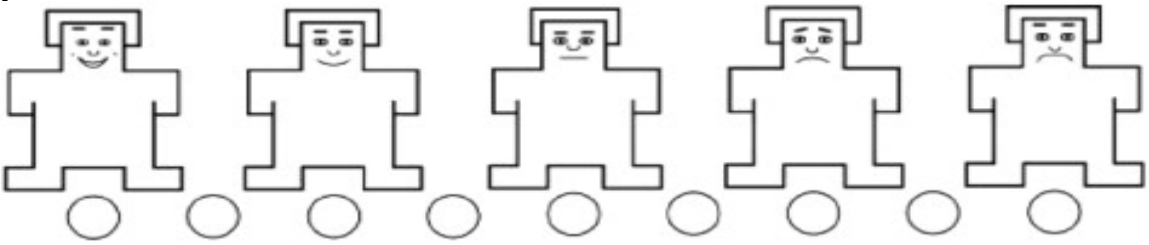
___ Never tried

Radishes



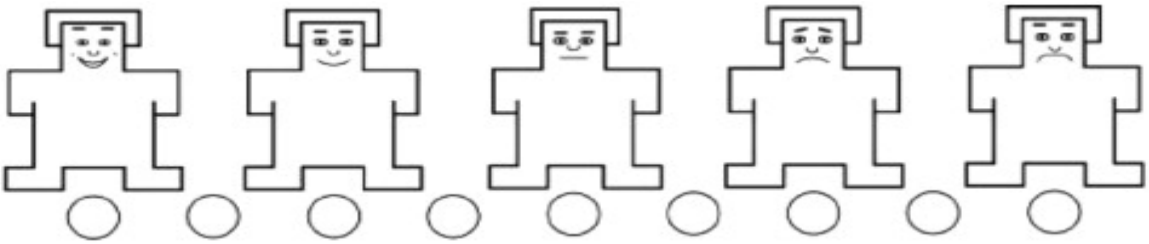
___ Never tried

Rye Bread



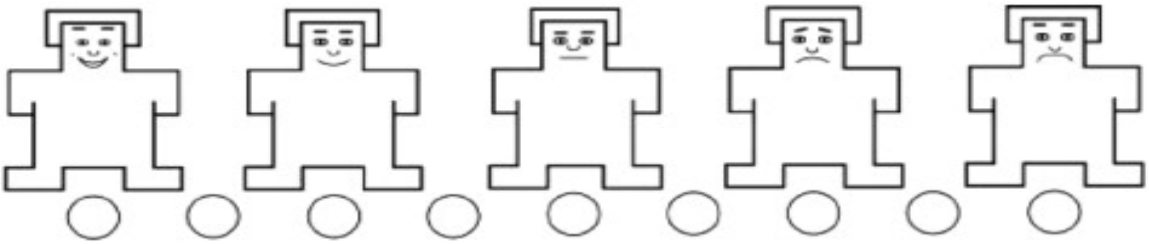
___ Never tried

Tea



___ Never tried

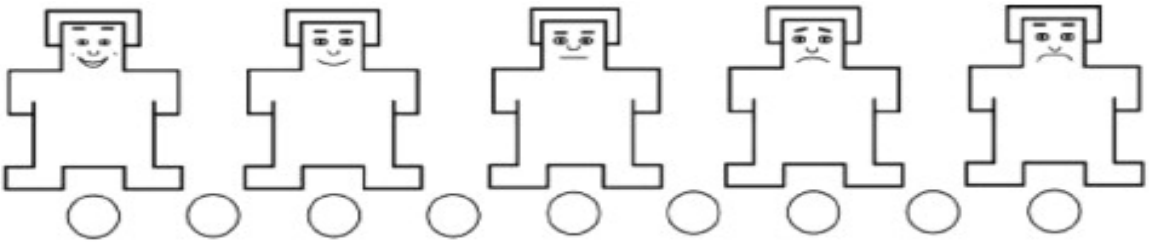
Tonic Water



___ Never tried

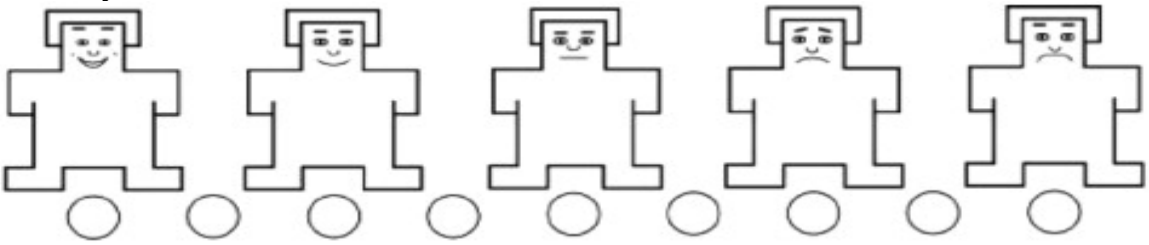
Salty items:

Bacon



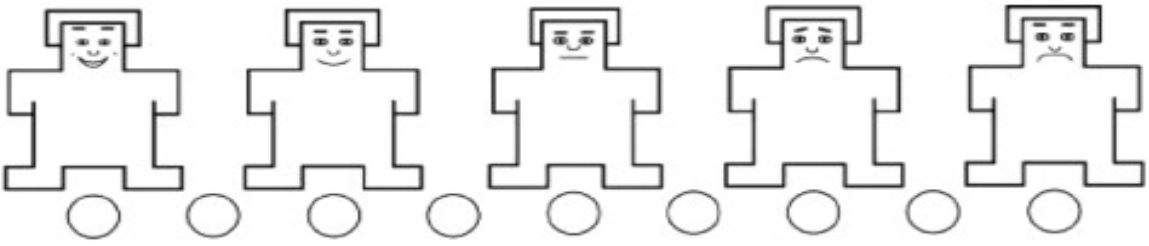
___ Never tried

Beef Jerky



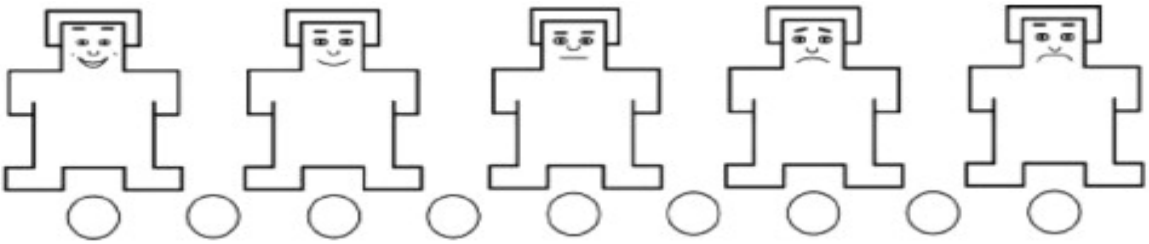
___ Never tried

Caviar



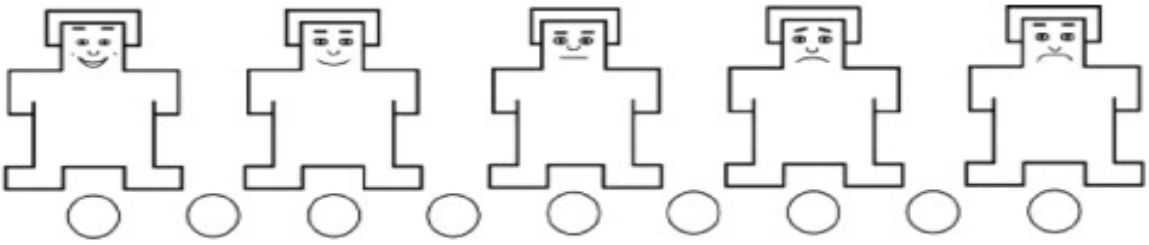
___ Never tried

Dill Pickles



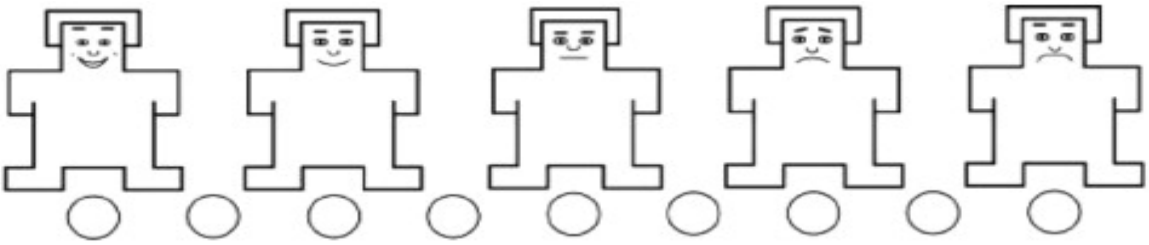
___ Never tried

Green Olives



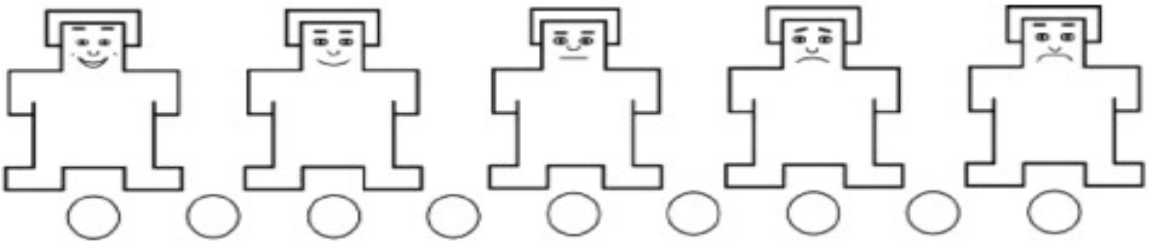
___ Never tried

Pretzels



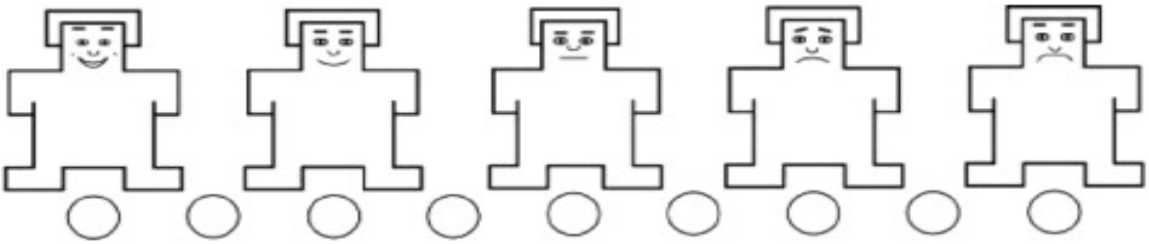
___ Never tried

Salt



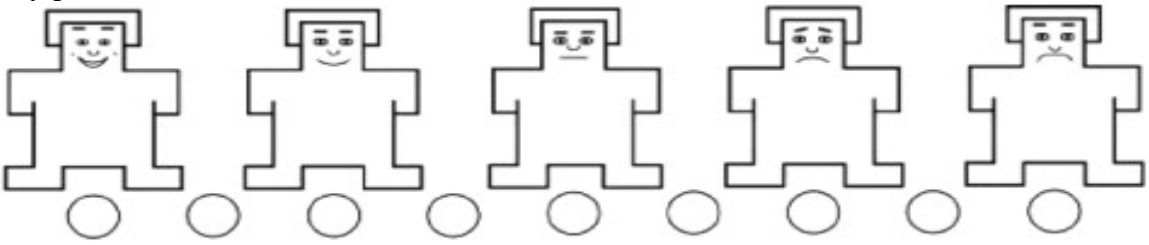
___ Never tried

Saltine Crackers



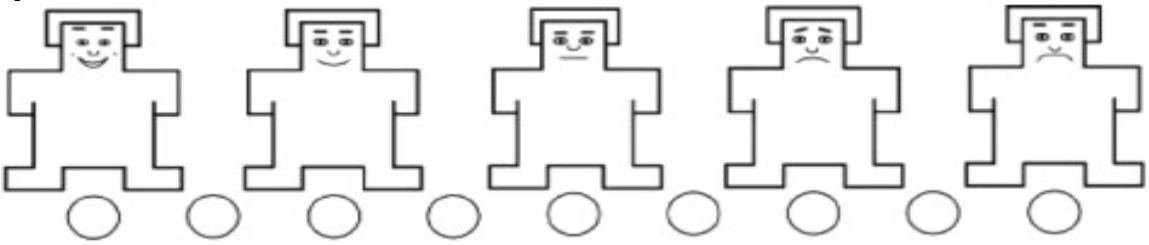
___ Never tried

Salty peanuts



___ Never tried

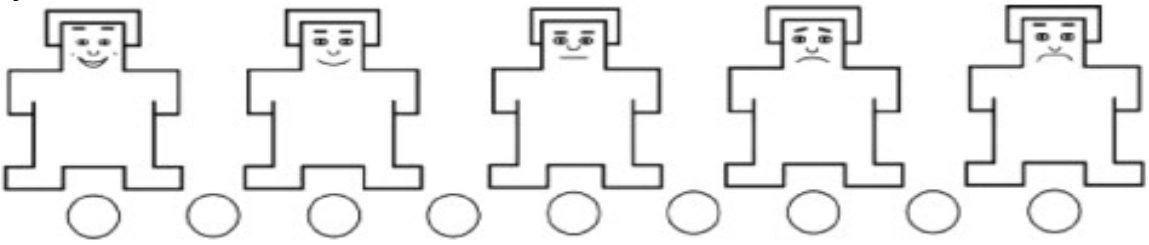
Soy Sauce



___ Never tried

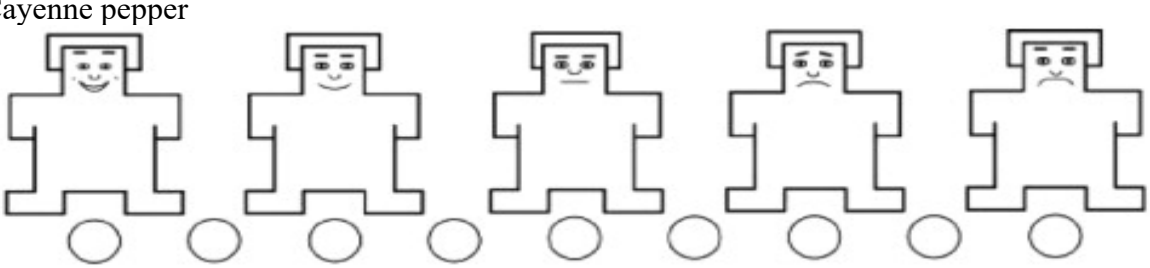
Spicy items:

Cajun foods



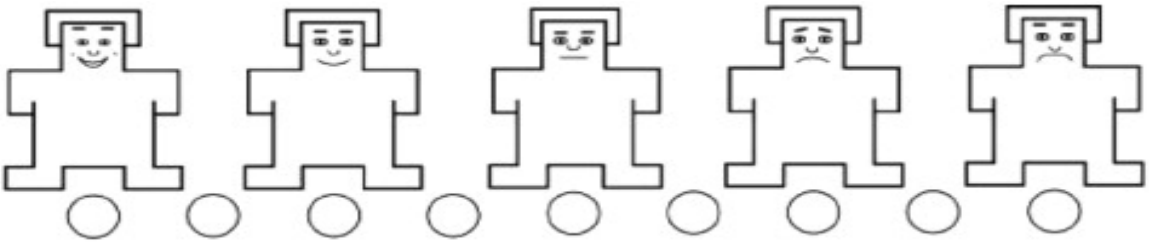
___ Never tried

Cayenne pepper



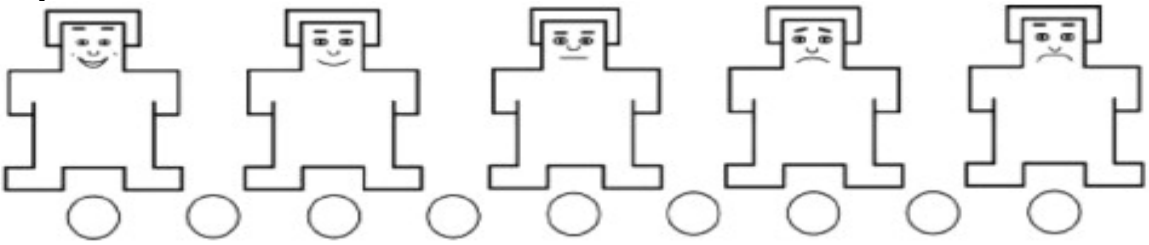
___ Never tried

Chilies



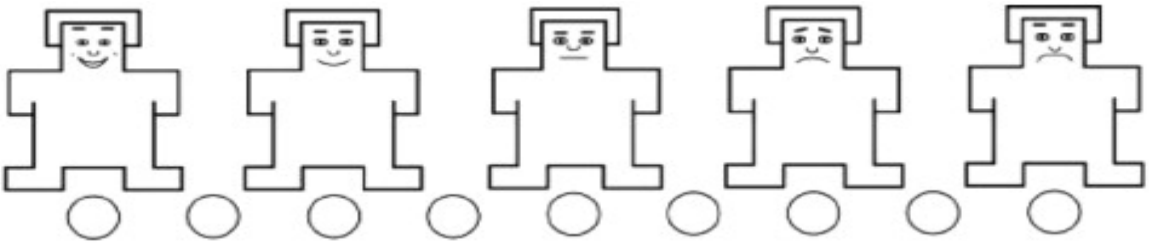
___ Never tried

Curry



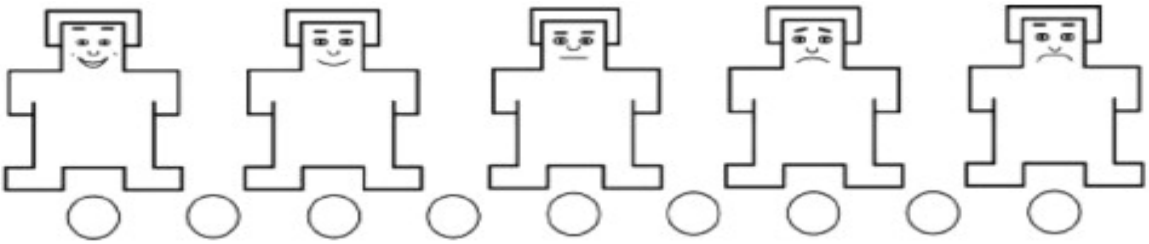
___ Never tried

Horseradish



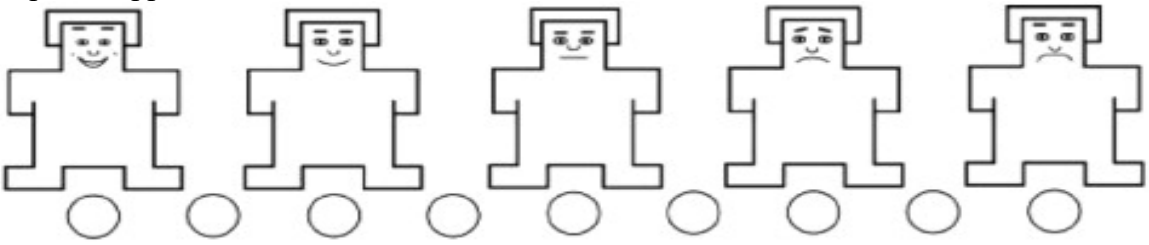
___ Never tried

Hot Salsa



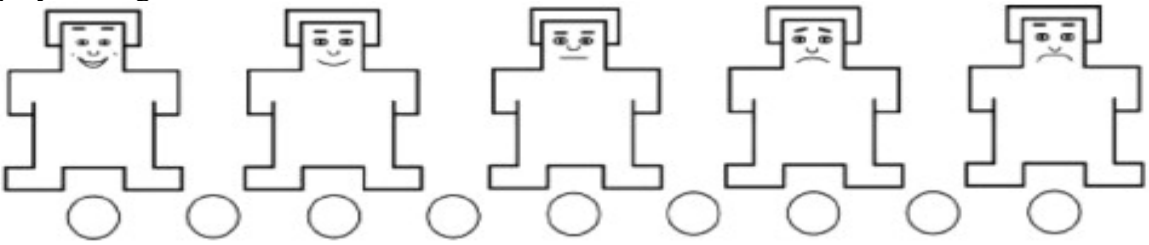
___ Never tried

Jalapeno Peppers



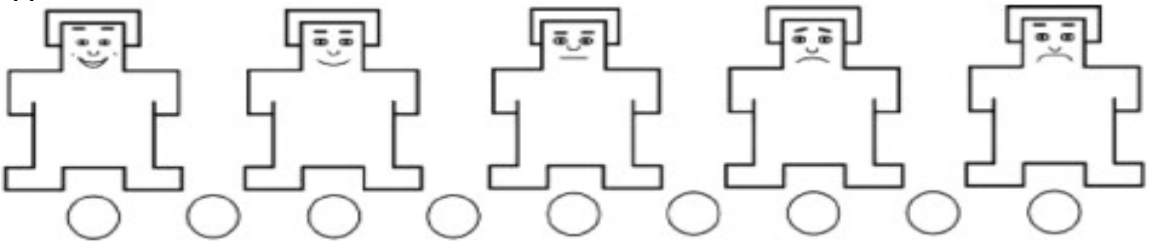
___ Never tried

Spicy Sausage



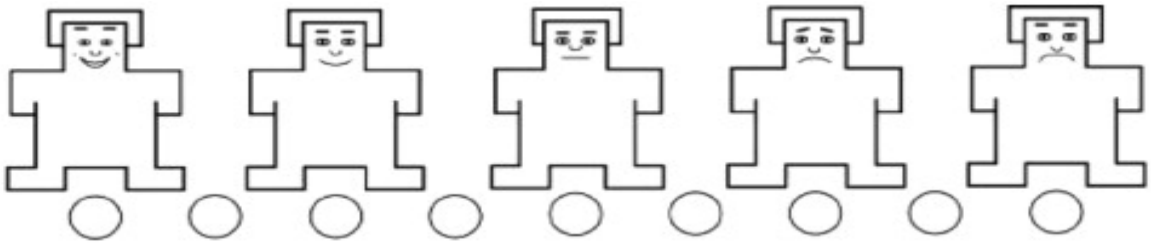
___ Never tried

Peppers



___ Never tried

Tabasco sauce



___ Never tried

Penn State Dependence on Electronic Cigarettes
Please check the answer that best applies to you.

1. How many times per day do you usually use your electronic cigarette (assume that one "time" consists of around 15 puffs or lasts around 10 minutes)?
   - ☐ 0-4 times/day
   - ☐ 5-9 times/day
   - ☐ 10-14 times/day
   - ☐ 15-19 times/day
   - ☐ 20-29 times/day
   - ☐ 30+ times/day

2. On the days that you can use your electronic cigarette freely, how soon after you wake up do you use your electronic cigarette?
   - ☐ 0-5 min
   - ☐ 6-15 min
   - ☐ 16-30 min
   - ☐ 31-60 min
   - ☐ 61-120 min
   - ☐ 121+ min

3. Do you sometimes awaken at night to use your electronic cigarette?
   - ☐ Yes
   - ☐ No

4. If yes, how many nights per week do you typically awaken to use your electronic cigarette?
   - ☐ 0–1 night
   - ☐ 2–3 nights
   - ☐ 4+ nights

5. Do you use an electronic cigarette now because it is really hard to quit?
   - ☐ Yes
   - ☐ No

6. Do you ever have strong cravings to use an electronic cigarette?
   - ☐ Yes
   - ☐ No

7. Over the past week, how strong have the urges to use an electronic cigarette been?
   - ☐ None/Slight
   - ☐ Moderate/Strong
   - ☐ Very Strong/Extremely Strong

8. Is it hard to keep using an electronic cigarette in places where you are not supposed to?
   - ☐ Yes
   - ☐ No

9. Did you feel more irritable because you couldn't use an electronic cigarette?
   - ☐ Yes
   - ☐ No

10. Did you feel nervous, restless, or anxious because you couldn't use an electronic cigarette?
    - ☐ Yes
    - ☐ No

PANAS

This measure consists of a number of words that describe different feelings and emotions. Read each item and then mark the appropriate response on the line next to the word. Indicate to what extent you have felt this way ***during the past week.***

Use the following scale to record your answers.

1	**2**	**3**	**4**	**5**
very slightly or not at all	a little	moderately	quite a bit	extremely

___interested	___irritable
___distressed	___alert
___excited	___ashamed
___upset	___inspired
___strong	___nervous
___guilty	___determined
___scared	___attentive
___hostile	___jittery
___enthusiastic	___active
___proud	___afraid

PURCHASE DECISION MAKING

You will now complete a series of decision-making tasks. You will be asked to make choices between different amounts of money given to you now or after a delay. These are hypothetical choices, but please choose your answer as if the items were to be delivered as described. Each task will start with some brief instructions on the screen. Read these instructions, and press the 5 key on the keyboard when you are ready to begin. There are no right or wrong answers in the tasks, just choose which option you prefer in each case. Please take your time and answer thoughtfully. To select the option on the left side of the screen, press the left arrow, and to select the option on the right side of the screen, press the right arrow. [Task implemented on computer via REDCap]

We are going to present you with a series of choices between amounts of money. For EACH pair, please select the ONE you would prefer…

Would you prefer…	**Yes?**	**OR**	**Yes?**
$54 today?		$55 in 117 days?	
$55 today?		$75 in 61 days?	
$19 today?		$25 in 53 days?	
$31 today?		$85 in 7 days?	
$14 today?		$25 in 19 days?	
$47 today?		$50 in 160 days?	
$15 today?		$35 in 13 days?	
$25 today?		$60 in 14 days?	
$78 today?		$80 in 162 days?	
$40 today?		$55 in 62 days?	
$11 today?		$30 in 7 days?	
$67 today?		$75 in 119 days?	
$34 today?		$35 in 186 days?	
$27 today?		$50 in 21 days?	
$69 today?		$85 in 91 days?	
$49 today?		$60 in 89 days?	

$80 today?		$85 in 157 days?	
$24 today?		$35 in 29 days?	
$33 today?		$80 in 14 days?	
$28 today?		$30 in 179 days?	
$34 today?		$50 in 30 days?	
$25 today?		$30 in 80 days?	
$41 today?		$75 in 20 days?	
$54 today?		$60 in 111 days?	
$54 today?		$80 in 30 days?	
$22 today?		$25 in 136 days?	
$20 today?		$55 in 7 days?	

Factors Influencing Purchases

When making purchase decisions around foods, beverages, and cosmetics, how much would you say each of these factors influence your decision to purchase a NEW product?

	Not at all	**A little**	**Somewhat**	**A lot**
1. Advertising				
2. Celebrity endorsement				
3. Packaging				
4. Price discount				
5. Recommendation from friends/family				
6. Smell				
7. Taste				

Self-Rated Sensory Ability

	Excellent	Very Good	Good	Fair	Poor
1. Overall, how would you rate your ability to smell?					
2. Overall, how would you rate your ability to taste?					

Sensory E-Cig Experiences Scale

	1 Strongly Agree	2	3	4	5	6	7 Strongly Disagree
1. I like the smell of the vapor.							
2. I like the taste of vaping.							
3. I like the feeling of creating vapor clouds.							
4. I like how creating vapor clouds looks visually appealing / cool.							
5. I like the flavor of vapor.							
6. I like how vaping makes me feel good physically.							
7. I like the feeling of satisfaction that I get from vaping.							
8. I like the feeling of pleasure that I get from vaping.							
9. I like doing vape tricks (e.g. Blowing vapor clouds or shapes like rings).							

PROMIS-E

	0 Never	**1**	**2**	**3**	**4 Almost Always**
1. I find myself reaching for my e-cigarette without thinking about it.					
2. I drop everything to go out and buy e-cigarettes or e-juice.					
3. I vape more before going into a situation where vaping is not allowed.					
4. When I haven't been able to vape for a few hours, the craving gets intolerable.					

SHRI-E
Vaping / using an e-cigarette/JUULing is something…

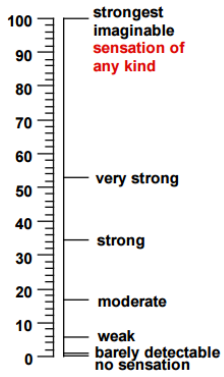
	1 Agree	**2**	**3**	**4**	**5**	**6**	**7 Disagree**
1. I do automatically.							
2. I do without having to consciously remember.							
3. I do without thinking.							
4. I start doing before I realize I'm doing it.							
5. I would find hard not to do.							
6. That is typically "me".							

Wattage: Research coordinator records wattage

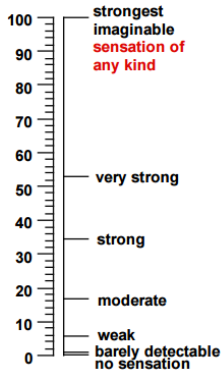
Generalized Magnitude Scale

For each item, please indicate how you would describe the E-CIG you just used by placing a mark on the verticle numbered line.

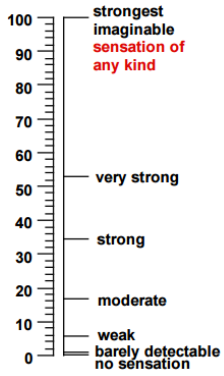
1. How would you describe the overall flavor sensation of the e-cig you just used?



2. How would you describe the overall harshness/irritancy of the ECIG you just used?

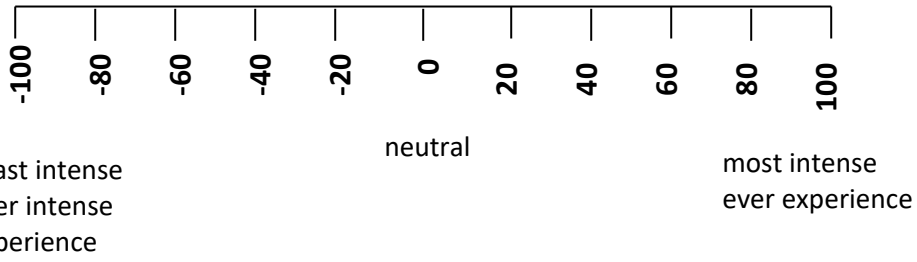


3. How would you describe the throat hit (sensation in the throat) of the ECIG you just used?

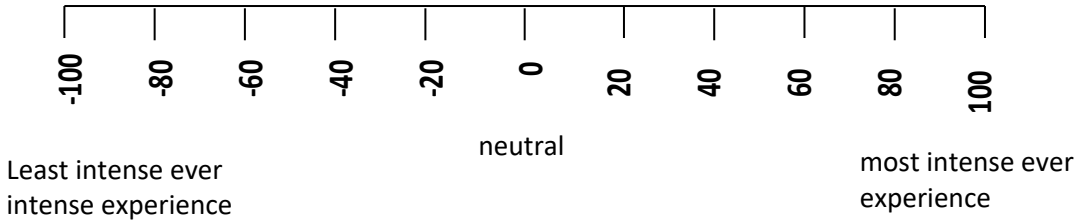


You will be presented with vials of liquid, each of which has a characteristic flavor. Please rate the taste on the following characteristics, where -100 is the least intense ever experience, 0 is neutral, and +100 is the most intense ever experience:

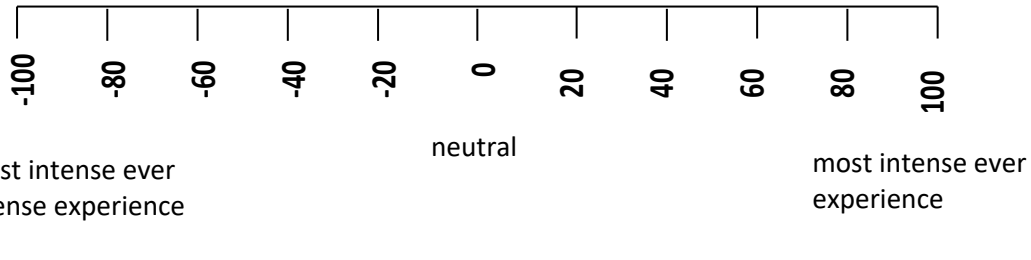
Pleasantness



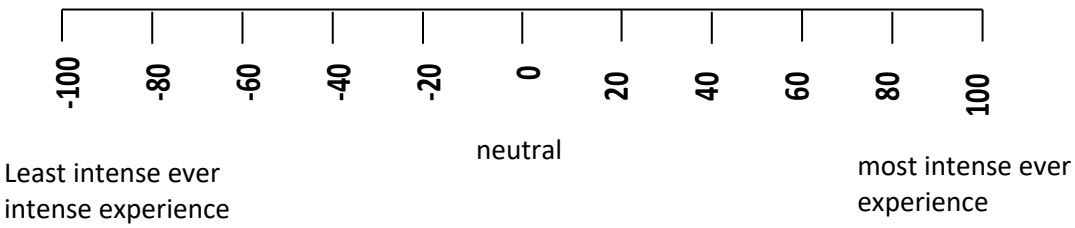
Irritation



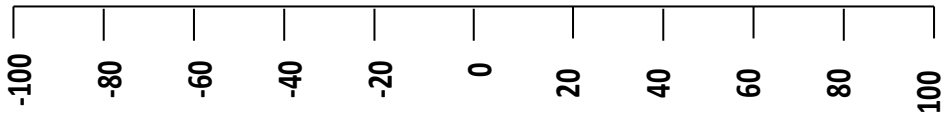
Relaxing



Satisfying



Sweet

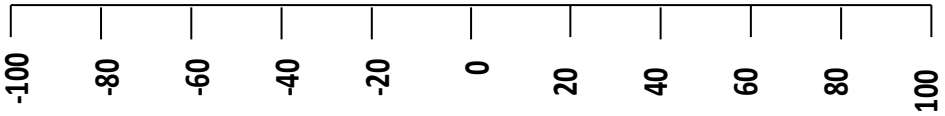


neutral

Least intense ever intense experience

most intense ever experience

Sour

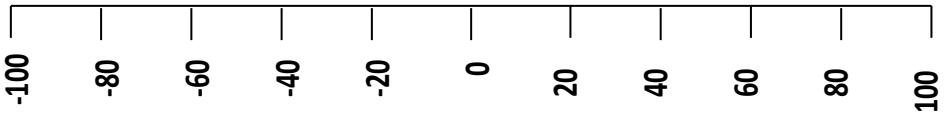


neutral

Least intense ever intense experience

most intense ever experience

Bitter

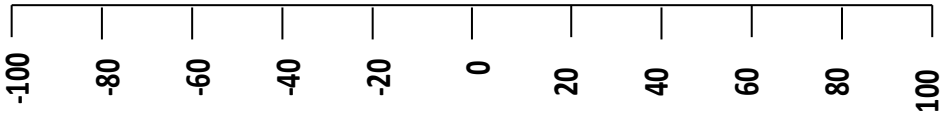


neutral

Least intense ever intense experience

most intense ever experience

Cool/cooling

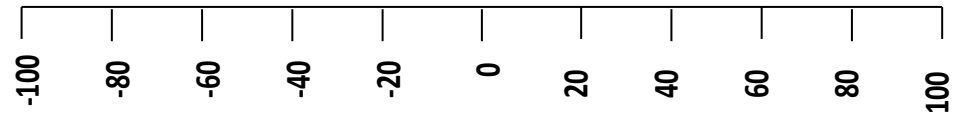


neutral

Least intense ever intense experience

most intense ever experience

Sharp/biting/astringent/pungent



neutral

Least intense ever intense experience

most intense ever experience

Duke Sensory Evaluation

Please rate the puffs you just took.

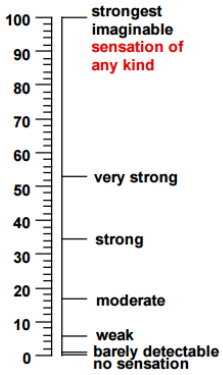
	1 Not at all	**2**	**3**	**4**	**5**	**6**	**7 Extremely**
1. How much did you like the puffs you just took?							
2. How satisfying were the puffs you just took?							
3. How high in nicotine do you think the puffs were?							
4. How similar to your own brand were the puffs?							
5. Strength of puffs on tongue?							
6. Strength of puffs in nose?							
7. Strength of puffs in back of throat?							

	1 Not at all	**2**	**3**	**4**	**5**	**6**	**7 Extremely**
8. Strength of puffs in windpipe?							
9. Strength of puffs in chest?							

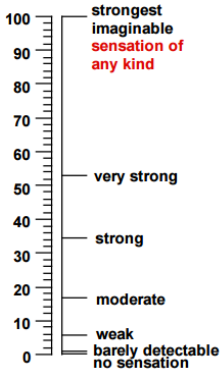
Hedonic Attribute Scale

For each item, please indicate how you would describe the ECIG you just used by placing a mark on the vertical numbered line.

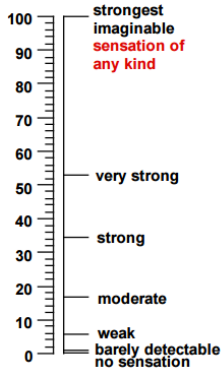
1. Draw



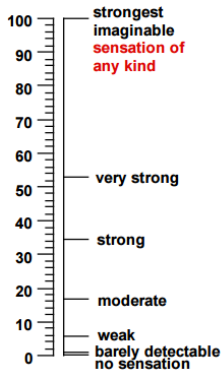
2. Mouthful of vapor



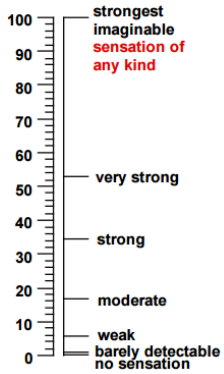
3. Visible vapor



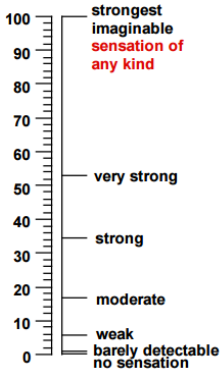
4. Smell



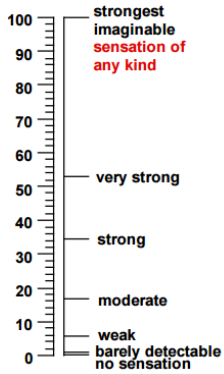
5. Impact



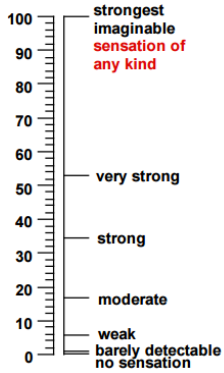
6. Irritation



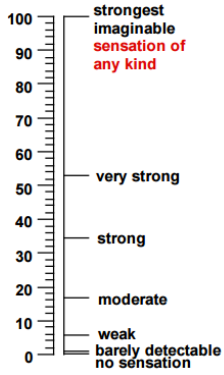
7. Strength



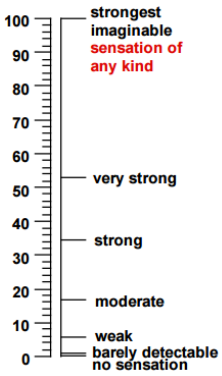
8. Smoothness



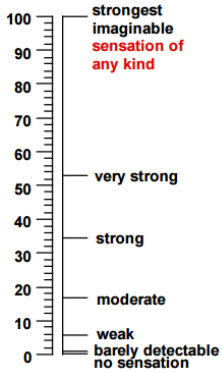
9. Taste



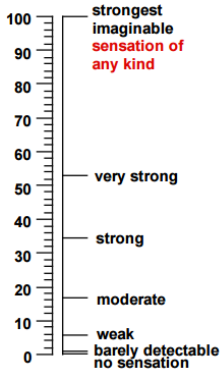
10. Aftertaste



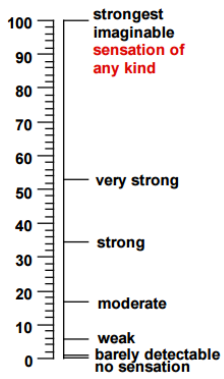
11. Throat hit



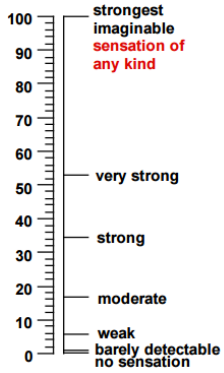
12. Dryness



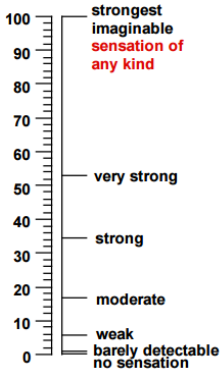
13. Tingling



14. Burning



15. Similarity to usual brand

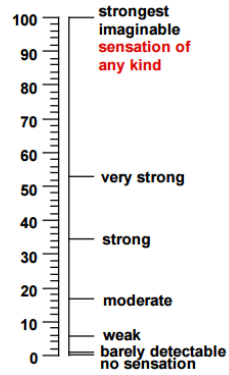


[leave blanks for 3 additional participant-supplied descriptors with gLMS scoring]

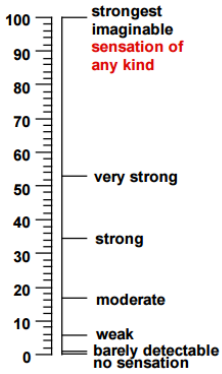
Drug Effects / Liking

Place a vertical line at the point on the scale that indicates how you feel about each of the statements right now.

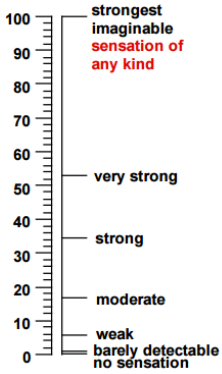
1. Do you feel any study product effects?



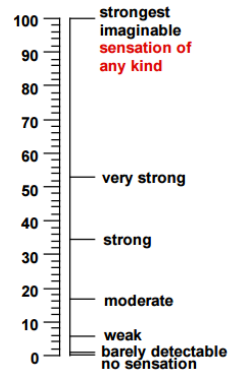
2. Do you feel any good study product effects?



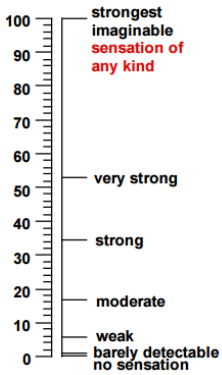
3. Do you feel any bad study product effects?



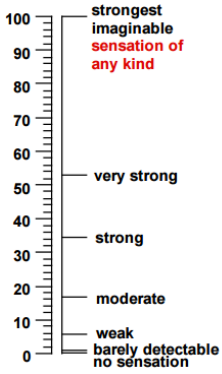
4. How much do you like the study product?



5. How much do you desire the study product?



6. How much would you like to use this product again?



Product Evaluation Scale.

Using the number scale below, answer the following questions regarding **the product you just used.**

Product Code: _____

	1 Not at all	**2 Very little**	**3 A little**	**4 Moderately**	**5 A lot**	**6 Quite a lot**	**7 Extremely**
1. Was it satisfying?							
2. Did it taste good?							
3. Did it make you dizzy?							
4. Did it calm you down?							
5. Did it help you concentrate?							
6. Did it make you feel more awake?							
7. Did it reduce your hunger for food?							
8. Did it make you nauseated?							
9. Did it make you feel less irritable?							
10. Did you enjoy the sensations in your mouth?							
11. Did it immediately reduce your craving for an e-cigarette?							
12. Did it relieve withdrawal symptoms?							

	1 Not at all	**2 Very little**	**3 A little**	**4 Moderately**	**5 A lot**	**6 Quite a lot**	**7 Extremely**
13. Did it relieve the urge to vape?							
14. Was it enough nicotine?							
15. Was it too much nicotine?							
16. Was it easy to use?							
17. Were there bothersome side effects?							
18. Would you be comfortable using the product in public?							
19. Did you still have a craving for an e-cigarette after using the product?							
20. Are you concerned you would become dependent on the product?							
21. Did you enjoy using the product?							
22. Would you be willing to use the product long term?							

Minnesota Tobacco Withdrawal Scale

How are you feeling at this very moment? **Please mark an (X) in ONE box for each condition**					
	Not at all	**Slightly**	**Somewhat**	**Very**	**Extremely**
Depressed	☐	☐	☐	☐	☐
Irritable	☐	☐	☐	☐	☐
Anxious /nervous	☐	☐	☐	☐	☐
Restless	☐	☐	☐	☐	☐
Dizziness	☐	☐	☐	☐	☐
Hungry	☐	☐	☐	☐	☐
Nausea	☐	☐	☐	☐	☐
Poor concentration	☐	☐	☐	☐	☐

How dangerous to your health did you find the ENDS product and solution comparedto your regular device and solution? (please mark an (X) on ONE of the boxes)

1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**

Compared to other smokers your age, what do you believe your risk is for developing thefollowing health problems? Would you say that you are…

5-point Likert Scale: 1 = Much Less Likely at Risk; 2 = Less Likely at Risk; 3 = About the samerisk; 4 = more likely at risk; 5 = much more likely at risk

1. Lung Cancer
2. Emphysema
3. Bronchitis
4. Other cancers
5. Heart disease
6. Addiction
7. Stroke
8. Mouth Cancer
9. Tooth Loss
10. Gum Disease

Screening: Oral Health

1. How often do you brush your teeth?
   [ ] Never
   [ ] 2 times a day
   [ ] < once a week
   [ ] 3 times a day
   [ ] 1-2 times a week
   [ ] > 3 times a day
   [ ] Every other day
   [ ] Once a day
   [ ] Don't know
   [ ] Refused

2. What material do you use with the toothbrush?
   [ ] Nothing
   [ ] Toothpaste
   [ ] Other_____(Specify) let participant write in answer if selected
   [ ] Don't know
   [ ] Refused

3. Do your gums bleed when you wash your teeth?
   [ ] No
   [ ] Sometimes
   [ ] Always or almost always
   [ ] Don't know
   [ ] Refused

4. How often do you use mouthwashes?
   [ ] Never
   [ ] 2 times a day
   [ ] < once a week
   [ ] 3 times a day
   [ ] 1-2 times a week
   [ ]> 3 times a day
   [ ] Every other day
   [ ] Once a day
   [ ] Don't know [ ] Refused

5. How many natural teeth do you have? (The adult mouth normally has 32 teeth, 16 on top and16 on bottom).
   [ ]_____(subtract from 32 the number of missing or artificial teeth)
   [ ] Don't know
   [ ] Refused

6. Do you have any removable dentures? Choose all that apply (can choose more than one)
   [ ] a partial denture
   [ ] a full upper denture
   [ ] a full lower denture
   [ ] Don't know
   [ ] Refused

7. About how long has it been since you last visited a dentist? Include all types of dentists, such as orthodontists, oral surgeons, and all other dental specialists, as well as dental hygienists.
[ ] Between 1 – 6 months
[ ] Between 6 – 12 months
[ ] More than 1 year ago
[ ] Never seen a dentist
[ ] Don't know
[ ] Refused

8. Do you have any fillings?
[ ] Yes. If yes, how many fillings? let participant write in answer if selected
[ ] No
[ ] Don't know
[ ] Refused

9. Have you taken any antibiotic medications in the last month?
[ ] Yes, but not currently
[ ] Yes, currently
[ ] No
[ ] Don't know
[ ] Refused

10. Do you currently take an inhaled corticosteroid (e.g. Beclomethasone dipropionate (Qvar), Budesonide (Pulmicort), Budesonide/Formoterol (Symbicort), Fluticasone (Flovent),Fluticasone INH powder (Arnuity Ellipta)?
[ ] Yes
[ ] No
[ ] Don't know

The next 5 items have response options of Never, Occasionally, and Often.

1. My mouth feels dry when eating a meal.
2. My mouth feels dry.
3. I have difficulty in eating dry foods.
4. I have difficulties swallowing certain foods.
5. My lips feel dry.

Please rate the product you used today on the following effects (0 – 100 VAS)

- Dry Mouth
- Excessive Salivation
- Mouth Irritation
- Throat Irritation
- Sharpness/cut
- Cough
- Phlegm
- Burning Sensation in Mouth
- Burning Sensation in throat
- Burning sensation on lip/gum
- Mouth Tingling
- Teeth Sensitivity

How likely are you to purchase [product selected above] in the next month?

10 = Certain, practically certain

9 = Almost sure

8 = Very probable

7 = Probable

6 = Good possibility

5 = Fairly good possibility

4 = Fair possibility

3 = Some possibility

2 = Slight possibility

1 = Very slight possibility

0 = No chance, almost no chance

Appendix D Sample Collection Procedures

Saliva Sample

Step 1. Open foil pouch and remove the Saliva Collection Aid (SCA)

Step 2. Place ribbed-end of the SCA securely into a pre-labeled collectionvial

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

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

Step 5. After collection, freeze samples at or below -20ºC.

Step 6. For Analysis, follow Salimetrics SOP for corresponding ELISA kit.

OPTIONAL Oral Rinse Sample (collected at Roswell Park only)

Supplies:

SCOPE® mouthwash: Travel size Scope mouthwash bottle is used to rinse mouth.

Saline solution: An alternative to Scope mouthwash, it will be used for participants with openoral ulcers or in recovering alcoholics concerned about the alcohol content.

Medicine cup: A 4.5 oz. sterile medicine cup used for pouring in the mouthwash.

Specimen container: A 5 oz. sterile specimen container used for spitting in the mouthwash andfor storing.

Gloves: The dental examiner will use a new pair of gloves before the exam begins.

Procedure:

1. Put on gloves and ask the participant: *"Do you have any sores in your mouth that might hurtwhen you use a mouthwash with some alcohol in it, such as Scope?"*

2. Pour 10mL of SCOPE® mouthwash, or the alternative saline solution, into a medicine cup,making sure not to touch the rim of the cup.

3. Hand the medicine cup with the mouthwash to the participant and explain to the participant: *"We are going to ask you to swish some Scope mouthwash around your mouth, gargle, and thenspit the mouthwash into a cup. First, you will rinse your mouth with the mouthwash for 5 seconds and then gargle for 5 seconds. You will do this three times and then spit the mouthwashinto a cup. Do you have any questions about this test?"*

4. Have the participant put the mouthwash, or saline, into their mouth when ready and theninstruct them through the swish gargle cycles using a timer.

5. At the end of the 30 seconds, open the specimen container and hand it to the participant. Holdthe top lid down to avoid contaminating it.

6. Have the participant spit the mouthwash into the specimen container when done gargling.Participants are allowed to touch the rim of the container when they spit the mouthwash.

7. Take the specimen collection cup from the participant being careful not to touch the rim.

8. Seal the specimen container properly to prevent leakage.

9. Place the participant label on the specimen collection container until processing

Appendix E Full Study Timeline

-15 min		PROP, PTC, Sodium Benzoate (1st session only) Saliva, Urine, Oral Samples (optional)
-10 min		Pre: Questionnaires
0 min		Begin *bout 1*
15 min		End *bout 1* / Collect Product
20 min		Post: Saliva
20 min		Post: Questionnaires
45 min		Begin *bout 2*
60 min		End *bout 2* / Collect Product
65 min		Post: Saliva
65 min		Post: Questionnaires