Cigarette Smoking Decision Study

NCT04595279

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JHM IRB - eForm A – Protocol

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1. Abstract

a. Provide no more than a one page research abstract briefly stating the problem, the research hypothesis, and the importance of the research.

The Family Smoking Prevention and Tobacco Control Act granted the FDA the authority to regulate and restrict tobacco advertising tactics that inaccurately convey reduced product risk, yet there is a dearth of up-to-date regulatory science to inform such regulations. Although the FDA has restricted use of descriptors such as “natural” and “additive-free,” research shows that the tobacco industry quickly pivoted to increase use of alternative, unregulated tactics. Greenwashing is one increasingly common tobacco marketing strategy in which products are portrayed as eco-friendly and/or natural. Our preliminary research indicates that greenwashing tactics may inaccurately convey modified product risk to consumers. The overarching objective of this project is to test the effect of greenwashing methods used by cigarette companies to market their products on actual smoking behavior in a controlled laboratory study. Our proposed research focuses on young adults (age 18-35), because this is a key age for smoking initiation and escalation, and research has found that young adults may be more susceptible than older adults to greenwashing in cigarette ads. This study will test the effect of greenwashing on behavioral economic demand and smoking topography in a laboratory-controlled cigarette self-administration study. These data will clearly connect tobacco advertising features to product risk perceptions and actual smoking behavior. This work will provide FDA with an integrated set of evidence that identifies misleading greenwashing tactics that inaccurately convey modified product risk which can be used to inform regulatory action regarding restrictions of this type of advertising.

2. Objectives (include all primary and secondary objectives)

The proposed double-blind laboratory study in 35 non-treatment seeking dependent smokers will determine the test the effect of greenwashing on behavioral economic self-administration and smoking topography. A within-subjects design will compare self-administration choice and smoking topography between two “brands” that in reality will be identical cigarettes with ads/labels that include vs. lack greenwashed tactics. Behavioral economic sessions will determine self-administration under concurrent availability of the two brands at various behavioral prices. Topography sessions will test ad-lib self-administration for each brand. Together, these sessions encompass the two primary ways advertising could affect smoking behavior (the amount smoked, and how one smokes). We hypothesize that greenwashed cigarettes will (a) show greater self-administration than non-greenwashed cigarettes when available at equivalent prices, (b) show reduced sensitivity to price compared to non-greenwashed cigarettes, and (c) will be self-administered more than non-greenwashed cigarettes even when their price is higher. We also hypothesize that in topography sessions greenwashed cigarettes will show: greater (a) total puff volume, (b) mean puff volume, (c) mean

puff duration, (d) mean maximum flow rate, (e) number of puffs; and lesser (f) mean inter-puff interval.

3. Background (briefly describe pre-clinical and clinical data, current experience with procedures, drug or device, and any other relevant information to justify the research)

The Family Smoking Prevention and Tobacco Control Act (FSPTCA) granted FDA the authority to regulate the tobacco product marketing and stop false or misleading advertising. Under the FSPTCA, tobacco companies are prevented from implicitly/explicitly conveying that a product is of modified risk, unless granted a permissive FDA order. In 2015, FDA issued warning letters to several tobacco companies regarding their use of the descriptors “natural” and “additive-free.” Underlying this action was research documenting that consumers inaccurately perceive cigarettes advertised with these descriptors to be lower risk than other cigarettes on the market (Gratale et al, 2019; Leas et al., 2016; Pearson et al., 2017). In early 2017, Santa Fe Natural Tobacco Company Inc. – manufacturer of Natural American Spirit (hereafter “American Spirit”) cigarettes and the largest such company – entered into a settlement agreement with the FDA that prohibited use of these terms (with the exception of the term “natural” in the product’s brand name).

However, the tobacco industry has a documented history of quickly pivoting to new tactics in the face of advertising restrictions. For example, when descriptors “light,” “low,” and “mild” were banned, the industry started using colors, and terms such as “smooth” and “fine”(Connolly & Alpert, 2014; King & Borland, 2005). More recently, evidence suggests that American Spirit advertisements have already adopted new tactics after the settlement agreement with FDA. Specifically, between 2016 (pre-settlement) and 2018 (post-settlement), prevalence of the phrase “tobacco and water‟ increased by 59% while prevalence of claims about the company’s ecofriendly behaviors increased 36%. This underscores the large arsenal of tactics companies use to mislead consumers to perceive a product as modified risk, as well as their ability to rapidly shift from one tactic to another. Identification of such strategies and evidence of their effect on risk perceptions and smoking behavior are needed to inform FDA‟s regulatory action.

Greenwashing is an increasingly common strategy deployed by the tobacco industry to portray products as less harmful. Greenwashing involves portraying a product or brand as eco-friendly and/or natural (Laufer, 2003). Ours and others’ work has found this is accomplished through a variety of lexical and graphical tactics (Epperson et al., 2017; 2018). Lexical tactics include (a) Textual descriptors (e.g., additive-free, natural, organic, pure) and (b) textual references (e.g., claims about sustainable farming, lack of pesticides, limited ingredients (e.g., “Tobacco & Water”), supplemental environmental activities (e.g., planting trees). Graphical tactics include the use of (a) specific icons (e.g., leaves, flowers, seeds, recycling symbols) and (b) broader settings and background imagery (e.g., farms, forests, wood or natural background). Studies across multiple domains of consumer products, including tobacco, demonstrate that greenwashed products are seen as healthier than products that are not marketed using greenwashed tactics (Byron et al., 2015; Lazzarini et al., 2016; O’Connor et al., 2017).

Behavioral economics, which bridges analysis from microeconomics with the methods and subject matter of behavioral science, examines how behavior is maintained by reinforcers under systems of constraint (Hursh, 1980, 1984). Demand analysis has been widely applied to human and animal drug reinforcement (Hursh et al., 2015; Johnson et al., 2004). Demand refers to the amount of reinforcer (e.g., cigarettes) consumed. Demand at various prices can be used to construct a demand curve, which can be quantified with specific metrics. Demand intensity is the person’s preferred level of consumption of that reinforcer when it is virtually free (at a trivial price). Demand elasticity refers to the sensitivity of reinforcer consumption in response to

changes in price (monetary price or behavioral price, i.e., how much effort is required to obtain the reinforcer).

A difference in any behavioral economic demand metric would be meaningful for the cigarette market, and traditional reinforcement measures do not examine all reinforcement aspects. For example, greater demand intensity for greenwashed compared to non-greenwashed cigarettes would indicate that greenwashing would increase cigarette consumption at the lower end of price ranges. Greater demand elasticity for greenwashed cigarettes compared to non-greenwashed cigarettes would indicate that greenwashing would increase cigarette consumption at higher prices in the commercial market, even if greenwashing had little or no effect at lower prices. Using progressive ratio breakpoint (a traditional reinforcement measure that corresponds to demand elasticity) would allow the study to miss meaningful differences in demand intensity. Using discrete choice (a traditional measure which typically uses a low price for both alternatives and is therefore analogous to demand intensity) would allow the study to miss difference in demand elasticity. Moreover, by examining reinforcer interactions (cross-price elasticity), demand analyses can inform the degree to which smokers would pay more for greenwashed cigarettes even if non-greenwashed cigarettes were available at a lower price. Therefore, the primary aims of the proposed study are to test the effect of greenwashing on behavioral economic self-administration measures. Additional topography measures will be conducted to determine smoking topography during ad-lib self-administration. Together, these sessions encompass the two primary ways advertising could affect smoking behavior (the amount smoked, and how one smokes).

4. Study Procedures

a. Study design, including the sequence and timing of study procedures (distinguish research procedures from those that are part of routine care).

Interested individuals will call the study contact number, and study personnel will conduct a brief screening for eligibility over the phone. To facilitate timely screening of participants for eligibility, website ads and flyers will contain a link to a brief online interest and eligibility survey using JHM Qualtrics. All individuals will be phone screened and, if qualified, scheduled for an in-person screening visit (approximately 2 hrs.) at the Behavioral Pharmacology Research Unit (BPRU) at the Johns Hopkins Bayview Medical Campus. Individuals will not sign consent before telephone screening. For those who meet phone screen eligibility, the laboratory screening will include physical and mental health history, drug history, physical examination, and standard laboratory tests of blood chemistry and hematology.

General Procedures: We will recruit and consent up to 100 individuals to accrue 35 non-treatment seeking male and female dependent cigarette smokers to complete the study by advertising and word-of-mouth. These volunteers will be medically healthy smokers without immediate intention to quit and will be fully informed community non-treatment seeking volunteers, who do not constitute a special vulnerable population. They will participate in a 9-session laboratory study at the Behavioral Pharmacology Research Unit at the Johns Hopkins Bayview Campus.

All lab visits will last approximately 4 hours total. Participants will be instructed to abstain from smoking for 6 hours before the beginning of each daily session in order to achieve a carbon monoxide (CO, a byproduct of smoking; measured by the Smokerlyzer, CoVita, Haddonfield, NJ, USA) measure ≤ 50% of the CO value obtained at the initial screening. If a participant fails to meet this criterion, the session will be rescheduled (or participation discontinued after multiple such instances). Sessions will be conducted at various times throughout the day, but each

individual participant will always begin his or her sessions at the same time of day throughout the experiment.

Greenwashing Manipulations (Sessions 1-9): During behavioral sessions participants will have the opportunity to smoke at least 1 of 2 types of cigarettes (topography sessions will involve the opportunity to smoke 1 type per session, whereas both types will be available during behavioral economic sessions and participants can choose to smoke either or both). Participants will be exposed to advertising for two different novel cigarette brands. One brand will be advertised using greenwashing tactics, while the other brand will have control advertising lacking the greenwashing tactics. To avoid a brand x greenwashing confound, the brand that is advertised with greenwashing materials will randomly vary across participants (e.g., Participant 1 may see Brand A advertised with greenwashing; Participant 2 may see Brand A advertised with the control ads). Participants will be exposed to the materials in two ways designed to replicate real world exposure to cigarette marketing for 30 minutes before sessions. First, posters will be placed on the walls to mimic advertising in retail settings. Participants will also be given printed information about each brand, designed to mimic direct mail advertisements, and may view this information as long as they like during the 30 minutes. These advertising materials and cigarette packs will remain in the room during topography and behavioral economic sessions. Unknown to the participants, both brands of cigarettes (Brand A and Brand B) will be the same commercial brand of cigarette. The study team will purchase cigarettes from a local store that sells commercially-available cigarettes. The study team will repackage these cigarettes into new packages that have either greenwashing elements or a control package that is similar, but without greenwashing elements. Although the two brand names and advertisements will be the same across participants, the actual commercial brand of cigarette used will be individualized for each participant to roughly the nicotine and menthol content for the participants typical brand of cigarettes. We will also ensure that it is a brand that lacks distinctive markings on the cigarettes that would allow for identification. Because this is within-subjects research that tests the effects of greenwashing, the brand used is arbitrary aside from the above considerations.

Topography sessions (Sessions 1-2): After assuring ≥6 hours of smoking abstinence via breath CO requirements, participants will take part in a 3-hour smoking topography session. In one session participants will have the ability smoke cigarettes associated with the greenwashing techniques, and in the other session participants will have the ability to smoke control cigarettes without the greenwashing technique used in labelling. Order of the two sessions will be randomized and counterbalanced across participants. Participants will be free to smoke cigarettes ad lib and in any manner they choose (e.g., depth and timing of inhalations) so long as they smoke the cigarettes through the small cigarette holder connected to our existing topography equipment (currently in use for IRB00107178). From this 3-hour session, topography measures to be determined include: total puff volume, mean puff volume, mean puff duration, mean inter-puff interval, mean maximum flow rate, and number of puffs.

At the conclusion of the second topography session, participants will practice the targeted puff volume smoking required of the following behavioral economic sessions. In contrast to the topography sessions, the behavioral economic sessions will require participants to achieve a target puff volume (70 ml) when they choose to self-administer cigarette puffs. This is because it is necessary to standardize puffs to ensure a constant reinforcer size across conditions. Product appeal will be assessed for both packages during these sessions.

Behavioral economics sessions (Sessions 3-9): In general, methods are modeled closely after those currently in place for research being conducted investigating reduced-nicotine

cigarettes in our laboratory (IRB00107178). In 4 sessions, a demand curve will be generated for greenwashed cigarettes while control cigarettes will be available at a fixed price throughout. Specifically, in one session, both types of cigarettes will be concurrently available for the same fixed, low behavioral price (10 plunger pulls for a bout of 3 cigarette puffs). In the other 3 sessions, the control cigarettes will be available for 10 pulls, while the greenwashed cigarettes will be concurrently available for 100, 1000, or 10000 pulls (varying across the 3 sessions). This models the realistic situations in which greenwashed cigarettes are available at higher prices than other cigarettes. Then in another 3 sessions which provide an important comparison condition, we will assess the opposite situation, in which price for control cigarettes is 100, 1000, or 10000 pulls across sessions (the session in which both are available for 10 pulls will have already been conducted), and greenwashed cigarettes are available at a fixed price of 10 pulls throughout. The order of the 7 behavioral sessions (with different price combinations) will be randomized for each participant.

During sessions, after confirming the CO breath requirement, the participant will take 1 puff of each type of cigarette. A 3 hour self-administration session will start 30 minutes after the initial puffs. Initial puffs will standardize the time since last smoking across all participants and sessions. Participants will complete each session in 1 of 4 existing identical ventilated smoking rooms, each equipped with a computer connected to a response console used to collect data. The console will have two Lindsley-type response plungers (custom modeled after Gerbrands No. G6310, Ralph Gerbrands Co., Arlington, MA, USA) horizontally spaced equidistantly along the front of the console. A force of 20 N will be required to operate the plunger and register a response. Depending on the response requirement of the session, a certain number of plunger pulls will result in controlled self-administration of cigarette puffs (described in more detail in puffing procedure subsection below). Either the left or right side plunger will be randomly associated across participants with either the greenwashed or control cigarettes. We will supply all cigarettes.

Puffing procedure for behavioral economic methods: At the start of each session, the participant will be instructed on puffing procedures, and will be given direct verbal feedback by a research assistant. Participants will also be given an instruction sheet specifying the ratio requirement (number of plunger pulls) required to receive access to puffs. Whenever a response requirement is met, the participant will smoke three puffs from earned cigarette type according to a standard smoking procedure. Specifically, after completion of the required ratio, the 180 second consumption period will begin. The computer will immediately show the message “Puff Now” and the computer will emit two tones. The participant will then take a new cigarette, light it without inhaling, put it in the holder, then inhale. This cigarette holder will cover the last 8 mm of the cigarette, and will be connected via two plastic tubes to a volumetric low pressure transducer designed to measure puff volume and duration through the computer. This system provides real-time feedback to participants on puff volume (ml units). When 60 ml is reached, the computer will then emit a tone. The participant will have been instructed during the training session (at end of 2nd topography session) to aim for 70 ml, and the tone at 60 ml will give enough time for the participant to react and cease inhaling at roughly 70 ml. During any one session, mean puff volume will be between 65 and 75 ml or the session will be repeated. The participant will hold the smoke for 5 seconds, when the computer will emit two tones, signaling exhale time. A 25 second inter-puff interval will then begin. After 25 seconds, “Puff Now” once again will appear and the cycle will begin again. After the tones signaling the participant to exhale are emitted for the third puff, an inter-trial interval will be maintained until 180 seconds have elapsed since ratio completion. Upon termination of this interval, the computer monitor will present, “You May Respond Now.”

Collection and storage of electronic information: All questionnaire material will be collected using JHM Qualtrics, and downloaded to a JH OneDrive folder. Study-related documents, including PHI, will only be stored and processed within a JH OneDrive folder or using computers owned by Hopkins. All such computers use full-disk encryption, OS- or app-level firewalls, anti-malware software, and are deployed in full compliance with JH standards.

Description of procedures to minimize risk during the COVID-19 pandemic: Although it is not possible to conduct sessions remotely due to the need to collect biological measures (e.g., blood samples) during screening and use of specialized equipment for experimental sessions (e.g., smoking and response apparatus), specific safety procedure will be put into place to minimize person-to-person contact in the context of the COVID-19 pandemic. First, all participants will be required to wear a properly fitting face surgical grade mask while in in the laboratory. The exception to this policy will be times in which the participant is alone in the test smoking rooms with the door closed. These rooms each contain independent, strong external exhaust systems. This exception is necessary because participants will be smoking study cigarettes while in the test rooms, which is not feasible or possible while wearing a face mask. Any participant that does not have a face mask will be provided one by the study team at no cost. Second, participants will be asked about potential COVID-19 symptoms upon arrival to the laboratory. Any subjects reporting symptoms indicative of COVID-19 per the JHU Clinical screening algorithm will be required to return home and participation will be paused for at least 2 weeks after which a health care professional must clear a return to participation (e.g., with a negative COVID-19 test). Third, appointment times will be staggered such that multiple participants will not be in the main laboratory room at the same time. Fourth, all equipment and surfaces will be wiped down following each session as well as at the beginning of each day with disinfectant (e.g., alcohol-based wipes or spray containing at least 70% alcohol to disinfect). Finally, all study staff will be required to wear properly fitting face masks while in the laboratory. Additionally, study staff will be required to wear a face shield for all times they are interacting within 6 feet of research participants. These procedures are successfully in place for an ongoing study in our laboratory using similar experimental procedures (IRB00107178).

b. Study duration and number of study visits required of research participants.

The total study duration will be approximately 2-3 weeks, depending on scheduling constraints, which is similar to ongoing studies in our laboratory. The total number of visits required will be 10 in person sessions. The screening session will last approximately 2 hours, and experimental session will last approximately 4 hours. If an unforeseen issue arises during session (e.g., fire alarm, technical difficulties), or a participant does not follow study protocol (e.g., does not abstain from smoking prior to session) participants may be asked to repeat a session.

c. Blinding, including justification for blinding or not blinding the trial, if applicable.

Volunteers will be blind to the fact that the same brand is used for both greenwashing and non-greenwashing conditions. Blinding is routine in human psychopharmacology studies, as it serves to minimize the confounding of data by expectations. It is not possible to blind volunteers and research staff from the greenwashing condition given the visual presentation of posters and flyers in the laboratory.

d. Justification of why participants will not receive routine care or will have current therapy stopped.

N/A. This study does not involve therapy.

e. Justification for inclusion of a placebo or non-treatment group.

N/A. This study does not involve placebo.

f. Definition of treatment failure or participant removal criteria.

Participants will be removed from this study if they fail to comply with protocol instructions that are outlined in the consent form or if they are not medically or psychologically suitable to continue.

g. Description of what happens to participants receiving therapy when study ends or if a participant's participation in the study ends prematurely.

The study procedures are not designed to provide therapy for cigarette smoking related problems. Participants will be individuals who do not have immediate plans to quit smoking.

5. Inclusion/Exclusion Criteria

Study Inclusion Criteria

- Participants must be between 18 and 35 years of age.
- Smoke at least five cigarettes per day
- Have an expired carbon monoxide level of more than 8 ppm or a urinary cotinine level of more than 100 ng per milliliter

Study Exclusion Criteria

Individuals will be excluded if they meet any of the following criteria as determined by screening:

- The intention to quit smoking in the next 30 days
- Use of "roll your own" cigarettes as an exclusive form of smoking
- A serious medical or psychiatric disorder or unstable condition
- Any positive toxicological screening for illicit drugs other than cannabis will be excluded
- Women who are pregnant, plan to become pregnant or are breast-feeding

6. Drugs/ Substances/ Devices

a. The rationale for choosing the drug and dose or for choosing the device to be used.

Both brands of cigarettes (Brand A and Brand B) presented in this study will be the same commercial brand of cigarette. The study team will purchase cigarettes from a local store that sells commercially-available cigarettes. The study team will repackage these cigarettes into new packages that have either greenwashing elements or a control package that is similar, but without greenwashing elements. Although the two brand names and advertisements will be the same across participants, the actual brand of commercial cigarette used will be individualized for each participant to approximate the nicotine and menthol content for the participants typical brand of cigarettes. We will also ensure that it is a brand that lacks distinctive markings on the cigarettes that would allow for identification.

b. Justification and safety information if FDA approved drugs will be administered for non-FDA approved indications or if doses or routes of administration or participant populations are changed.

N/A

c. Justification and safety information if non-FDA approved drugs without an IND will be administered.

N/A

7. Study Statistics

a. Primary outcome variables.

Demand Metrics: Reinforcement will be assessed by the 2 essential demand metrics: demand intensity and demand elasticity; which are calculated with nonlinear regression using the exponential demand equation (Hursh & Silberberg, 2008). Auxiliary metrics (Pmax, Omax, breakpoint) will also be examined, although these are derivative of the essential metrics. Demand elasticity and demand intensity will be calculated for each cigarette type (greenwashed or control) as it escalates in price and the alternative cigarette price remains fixed. Cross-price elasticity will be calculated to quantify the effect of increasing greenwashed cigarette work requirements on control cigarette consumption, and vice-versa. These measures will indicate how greenwashing perceptions may increase smoking. Greater demand intensity for greenwashed cigarettes compared to nongreenwashed cigarettes would indicate that greenwashing would increase cigarette consumption even at the lower end of commercial price ranges. Greater demand elasticity for greenwashed cigarettes compared to nongreenwashed cigarettes would indicate that greenwashing would increase cigarette consumption at higher prices in the commercial market, even if greenwashing had little or no effect at lower prices. By examining reinforcer interactions (cross-price elasticity), demand analyses can inform the degree to which smokers would pay more for greenwashed cigarettes even if non-greenwashed cigarettes were available at a lower price.

b. Secondary outcome variables.

Smoking Topography: We will collect six measures of smoking topography: total puff volume, mean puff volume, mean puff duration, mean inter-puff interval, mean maximum flow rate, and number of puffs. These data will be collected by ad lib smoking using our existing custom smoking topography system currently in use in our laboratory (IRB00107178). Our current research uses this topography system to help participants achieve a target volume per puff, but is already fully functional in its ability to measure topography of ad lib smoking. These measures will indicate the effect of greenwashing on how people smoke cigarettes in more damaging ways, for example, by smoking more deeply (greater puff volume), faster (greater maximum flow rate, lower inter-puff interval), or with increased time in lungs (greater puff duration).

c. Statistical plan including sample size justification and interim data analysis.

Analysis of Demand Curves: A paired-samples *t*-test will examine each demand metric, with data transformations of each demand metric if non-normally distributed (square root transform of Q0 and natural-log transform of α). We expect different demand profiles (greater demand intensity, and lower elasticity of demand) when cigarettes are greenwashed compared to control cigarettes.

Analysis of Cross-Price Elasticity: To calculate cross price elasticity of cigarettes, any instances of zero self administrations within a block will be coded as 0.5 because the logarithm

of zero is undefined. Then, a linear regression will be performed on the log10 of consumption means vs. the log10 of unit prices. The resulting slope of this regression line will be the cross-price elasticity.

Analysis of Smoking Topography: Paired-samples *t*-tests will be used to compare measures of smoking topography between the greenwashed and control cigarettes.

Statistical power:
Using data from an ongoing operant demand study in our lab evaluating the substitutability of reduced-nicotine content cigarettes for full-nicotine cigarettes (grant R01DA042527), elasticity (α) of reduced-nicotine cigarettes was significantly greater than that of full-nicotine cigarettes (Cohen's d = 1.33). Although these analyses were limited to single-item demand (i.e. cigarettes not concurrently available), the same underlying principles are applicable to the current analysis. Assuming an effect size half as large (d=.67), a sample size of N = 20 would provide power ≥ 80% (two-tailed; α=.05) to detect a main effect of greenwashing tactics on demand metrics. Our proposed sample size of N = 35 would provide between 97-98% power in the current analyses comparing demand metrics between the cigarette packaging types, assuming an effect size of d=0.67 or 0.70, respectively. A previous study comparing smoking topography of water pipe tobacco with and without graphic warning labels demonstrated significantly reduced total puff volume in the water pipe with the graphic warning label relative to the unlabeled pipe (d=0.49) (Maziak et al., 2019). Using the effect size from Maziak et al. (2019), which is comparable to the current approach, a sample size of N = 35 would provide ≥80% power (two-tailed; α=.05). Because the published topography data represent the smallest encountered effect size among the outcomes, we are powering the study to address this effect, which will provide a sample size that is beyond sufficiently-powered to address the aforementioned demand outcomes.

Demand metrics (demand intensity, demand elasticity, cross-price elasticity) and topography measures (total puff volume, mean puff volume, mean puff duration, mean inter-puff interval, mean maximum flow rate, and total puff number) will be compared between control and greenwashed cigarettes using paired-samples *t*-tests. Power analyses were performed for all primary behavioral economic and topography variables. Because topography measures showed the smallest anticipated effect based on published data (d = 0.49), we have conservatively based our sample size on topography. Despite this conservative estimation, if non-significant trends are observed suggesting potential effects, the proposed research will provide excellent data for informing power for future studies.

d. Early stopping rules.

No interim analyses are planned. The investigators will monitor safety data and relevant literature and report information to the IRB that might increase the risk assessment of the study.

8. Risks

a. Medical risks, listing all procedures, their major and minor risks and expected frequency.

Because the study will use participants who currently smoke, the risks associated with cigarettes are slight. Cigarettes to be administered in this study are expected to produce discernible effects with minimal safety risk. Participants are unlikely to experience side effects during the research, although as with any study, some risks exist. The main risk is that participants may experience side effects through exposure to the cigarettes or from withdrawal

symptoms prior to smoking which may be unpleasant. These include dizziness, nausea, headache, cough, sore throat, increased heart rate, and increased blood pressure. Side-effects of the cigarettes would be temporary. Participants may also become tired or bored during the sessions.

For blood samples taken intravenously, there is a minor risk of problems associated with insertion of the needle, including local irritation, inflammation, bleeding, and chance of infection at the insertion sites. Breach of confidentiality about self-reported drug use and biological tests indicating recent drug use is also a risk.

b. Steps taken to minimize the risks.

Participants are not a vulnerable population as defined by human participants protection guidelines; that is, they are not minors, pregnant women, under legal coercion or restriction, or mentally impaired. They are competent adults who provide their voluntary informed consent. Participants will be recruited via advertisements that clearly state the nature and intent of the study. The consent process will inform the participant in detail of the procedures, time involvement, compensation, risk, and treatment options other than participation in our study. Particular emphasis will be given to providing information regarding the potential risks. Volunteers will also be instructed that they may discontinue participation at any time without penalty. Research assistants at BPRU are rigorously trained in conducting and monitoring behavioral pharmacology experiments, and are experienced with observing and rating effects of drugs. Expired air samples will be collected to test for the presence of alcohol (indicating current impairment), and sessions will not be conducted unless alcohol concentration in the breath test is 0.00%. If a participant appears to be under the influence of a drug upon arrival at the BPRU, the session will not be run.

Cigarettes provided in the present study are commercially available, and will be delivered to individuals who already smoke with no intention to quit, and therefore risk is minimal. Staff are alert and careful in the protection of participants from risks. In the unlikely event of a medical issue, a physician in our research unit, including our co-investigator Dr. Annie Umbricht, M.D., is always available via a dedicated emergency contact line. The medical and nursing staff at BPRU is trained in CPR. The PI and physician co-investigator will be immediately notified of any serious events that arise. These include accidents, or hospitalization episodes that occur while individuals are participating in the study. In any case in which a participant ceases study participation due to unlikely side effects the PI will make a detailed report to the IRB. Urine will be tested for evidence of recent drug use at screening and experimental sessions and any positive toxicological screening for illicit drugs other than cannabis will be exclusionary.

Additionally, following standard hospital practices will minimize risks associated with blood draws. To protect participant information, participants' names will be recorded only during the screening, informed consent, and on necessary medical forms. Anonymous participant identification numbers will be used on all other forms and labeling of biological fluids and test results. All information gathered will be kept in locked research staff offices or file cabinets. All medical information obtained will be handled in accordance with HIPAA regulations. Only research staff will have access to participant records. The limits of confidentiality (e.g., suspected child abuse or neglect, or harm to self or others) will be discussed in detail with the participants during the informed consent process.

c. Plan for reporting unanticipated problems or study deviations.

The principle investigator will be responsible for notifying the IRB if an unanticipated problem or study deviation occurs.

d. Legal risks such as the risks that would be associated with breach of confidentiality.

N/A

e. Financial risks to the participants.

Not applicable. There are no financial risks to study volunteers.

9. Benefits

a. Description of the probable benefits for the participant and for society.

There is no benefit for participants in this study other than financial compensation. This study will develop and provide clinically meaningful data on the impact of greenwashing advertisements, and will directly inform FDA policy.

10. Payment and Remuneration

a. Detail compensation for participants including possible total compensation, proposed bonus, and any proposed reductions or penalties for not completing the protocol.

For this study, participants will be provided $75 for screening and $50 for each experimental session thereafter with an additional $50 bonus earned for each experimental session for those who complete the study (up to 9 in-person laboratory experimental sessions including initial exposure sessions for a total $450 in bonus payments). This payment system provides an approximately equivalent compensation rate per visit as provided in a previous long-term laboratory studies (IRB00107178). Due to the substantial time given by each participant over the course of roughly 2-3 weeks, participants will be able to earn up to $975 for completing the study. Additionally, if a participant refers someone to the study who then completes the study, the referring participant will receive a one-time bonus payment of $200. This referral bonus will be retroactively applied to any referring participant who has previously completed the study.

11. Costs

a. Detail costs of study procedure(s) or drug (s) or substance(s) to participants and identify who will pay for them.

There will be no cost to study volunteers for participating in the study.

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