Document Coversheet

Study Title: Marijuana Effects on Simulated Driving Performance

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	IRB 12/26/23
NCT Number:	NCT03699540
IRB Number	43636
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Which IRB

(•) Medical ( ) NonMedical

Protocol Process Type

( ) Exemption
(•) Expedited (Must be risk level 1)
( ) Full

IMPORTANT NOTE: You will not be able to change your selections for "Which IRB" and "Protocol Process Type" after saving this section. If you select the wrong IRB or Protocol Process Type, you may need to create a new application.

See below for guidance on these options, or refer to ORI's "Getting Started" page. Please contact the Office of Research Integrity (ORI) at 859-257-9428 with any questions prior to saving your selections.

Which IRB

The **Medical IRB** reviews research from the Colleges of:

- Dentistry
- Health Sciences
- Medicine
- Nursing
- Pharmacy and Health Sciences
- and Public Health.

The **Nonmedical IRB** reviews research from the Colleges of:

- Agriculture
- Arts and Sciences
- Business and Economics
- Communication and Information
- Design; Education
- Fine Arts
- Law
- and Social Work

Note: Studies that involve administration of drugs, testing safety or effectiveness of medical devices, or invasive medical procedures must be reviewed by the **Medical IRB** regardless of the college from which the application originates.

Which Protocol Process Type

Under federal regulations, the IRB can process an application to conduct research involving human subjects in one of three ways:

- by exemption certification
- by expedited review.
- by full review;

The investigator makes the preliminary determination of the type of review for which a study is eligible. Please refer to ORI's "Getting Started" page for more information about which activities are eligible for each type of review.

The revised Common Rule expanded exemption certification category 4 for certain secondary research with identifiable information or biospecimens. The regulations no longer require the information or biospecimens to be existing. For more information see the Exemption Categories Tool.

PROJECT INFORMATION

0 unresolved comment(s)

Title of Project: (Use the exact title listed in the grant/contract application, if applicable).
If your research investigates any aspect of COVID-19, please include "COVID19" at the beginning of your Project Title and Short Title

Marijuana and Alcohol Effects on Simulated Driving Performance

Short Title Description
Please use a few key words to easily identify your study - this text will be displayed in the Dashboard listing for your study.

Marijuana Driving Study

Anticipated Ending Date of Research Project: 4/1/2025

Maximum number of human subjects (or records/specimens to be reviewed) 34

After approval, will the study be open to enrollment of new subjects or new data/specimen collection? ○ Yes ◉ No

Are you requesting that the UK IRB serve as the lead IRB for a multi-site study, or that the UK IRB defer review to another IRB? [Click here for "IRB Reliance" help]
○ Yes ◉ No
If "Yes," before completing your IRB application, fill out the Reliance Request Form and submit it to irbreliance@uky.edu.

RISK LEVEL

0 unresolved comment(s)

Indicate which of the categories listed below accurately describes this protocol

- (•) (Risk Level 1) Not greater than minimal risk
- ( ) (Risk Level 2) Greater than minimal risk, but presenting the prospect of direct benefit to individual subjects
- ( ) (Risk Level 3) Greater than minimal risk, no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.
- ( ) (Risk Level 4) Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of subjects.

*"Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests.

*****For Expedited and Exempt Applications, the research activities must be Risk Level 1 (no more than minimal risk to human subjects).*****

Refer to UK's guidance document on assessing the research risk for additional information.

SUBJECT DEMOGRAPHICS **0 unresolved comment(s)**

Age level of human subjects: (i.e., 6 mths.; 2yrs., etc..) 21 to 50

Study Population:

Describe the characteristics of the subject population, including age range, gender, ethnic background and health status. Identify the criteria for inclusion and exclusion.

Provide the following information:

- A description of the subject selection criteria and rationale for selection in terms of the scientific objectives and proposed study design;
- A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group;
- Justification for the inclusion of vulnerable groups such as children, prisoners, adults with impaired consent capacity, or others who may be vulnerable to coercion or undue influence.

Please consider these resources:
NIH Diversity Policy
FDA Diversity Guidance

Our goal is to have up to 24 volunteers complete the study. Based on previous studies our research group has completed at UK, we anticipate that we will have up to 100 subjects sign consent in order to complete this study. Written, sober informed consent will be obtained prior to enrollment, and subjects will be paid for their participation.

Inclusion criteria include: 1) male and female English-speaking literate adults, ages 21-50 years old, 2) current recreational marijuana use (range: approximately 2 occasions in the past 3 months; through everyday users); history of vaporized or smoked marijuana use, 3) observed urine sample testing positive for cannabinoids (e.g., THC), 4) current weekly drivers with a history of at least 2 years of driving, 5) current alcohol use of less than or equal to 12 out of the past 30 days, 6) history of drinking to intoxication or impairment; history of using marijuana to intoxication or impairment,7) not seeking treatment for drug or alcohol use, 8) if female, a negative pregnancy test and use of effective form of contraception during study participation (e.g., oral contraceptive, abstinence, barrier method), and 9) valid driver's license.

Exclusion criteria include: 1) physiologic drug dependence on opioids, benzodiazepines, barbiturates, and/or alcohol that would require medical management, 2) significant ongoing medical problems (e.g., diabetes); clinically significant acute medical problem or chronic medical problem requiring daily medication or ongoing care; medical conditions that could be exacerbated by drug exposure of interfere with study procedures, 3) history of seizure or clinically significant head trauma, 4) serious psychiatric illness outside of drug use (e.g., schizophrenia), 6) liver function tests greater than 2x the upper limits of normal range, 7) a known hypersensitivity to the study drugs (e.g., recent history of panic-like reaction after marijuana use), 8) currently pregnant, planning on becoming pregnant or breast feeding, 9) inability to tolerate the simulated driving environment (e.g., simulator sickness), or 10) recent use of CYP2C9 or CYP3A4 inhibitor or inducer.

Attachments

Indicate the targeted/planned enrollment of the following members of minority groups and their subpopulations. Possible demographic sources: Census Regional Analyst Edition, Kentucky Race/Ethnic Table, Kentucky Population Data.
(Please note: The IRB will expect this information to be reported at Continuation Review time for Pre-2019 FDA-regulated Expedited review and Full review applications):

Participant Demographics

	Cisgender Man	Cisgender Woman	TGNB/TGE	Unknown/Not Reported
American Indian/Alaskan Native:	0	0		
Asian:	3	3		
Black/African American:	23	15		
Latinx:				
Native Hawaiian/Pacific Islander:				
White:	25	25		
American Arab/Middle Eastern/North African:				
Indigenous People Around the World:				
More than One Race:				
Unknown or Not Reported:	3	3		

If unknown, please explain why:

Indicate the categories of subjects and controls to be included in the study. You may be required to complete additional forms depending on the subject categories which apply to your research. If the study does not involve direct intervention or direct interaction with subjects, (e.g., record-review research, outcomes registries), do not check populations which the research does not specifically target. For example: a large record review of a diverse population may incidentally include a prisoner or an international citizen, but you should not check those categories if the focus of the study has nothing to do with that status.

Check All That Apply (at least one item must be selected)

- ☐ Children (individuals under age 18)
- ☐ Wards of the State (Children)
- ☐ Emancipated Minors
- ☐ Students
- ☐ College of Medicine Students
- ☐ UK Medical Center Residents or House Officers
- ☐ Impaired Consent Capacity Adults
- ☐ Pregnant Women/Neonates/Fetal Material
- ☐ Prisoners
- ☐ Non-English Speaking (translated long or short form)
- ☐ International Citizens
- ☑ Normal Volunteers
- ☐ Military Personnel and/or DoD Civilian Employees
- ☐ Patients
- ☐ Appalachian Population

ADDITIONAL INFORMATION:

Please visit the IRB Survival Handbook for more information on:

- Children/Emancipated Minors
- Students as Subjects
- Prisoners
- Impaired Consent Capacity Adults
- Economically or Educationally Disadvantaged Persons

Other Resources:

- UKMC Residents or House Officers [see requirement of GME]
- Non-English Speaking [see also the E-IRB Research Description section on this same topic]
- International Citizens [DoD SOP may apply]
- Military Personnel and/or DoD Civilian Employees

Assessment of the potential recruitment of subjects with impaired consent capacity (or likelihood):

☐ Check this box if your study does NOT involve direct intervention or direct interaction with subjects (e.g., record-review research, secondary data analysis). If there is no direct intervention/interaction you will not need to answer the impaired consent capacity questions.

Does this study focus on adult subjects with any conditions that present a high *likelihood* of impaired consent capacity or *fluctuations* in consent capacity? (see examples below)

○ Yes ◉ No

If Yes and you are not filing for exemption certification, go to "Form T", complete the form, and attach it using the button below.

Examples of such conditions include:

- Traumatic brain injury or acquired brain injury
- Severe depressive disorders or Bipolar disorders
- Schizophrenia or other mental disorders that involve serious cognitive disturbances
- Stroke
- Developmental disabilities
- Degenerative dementias
- CNS cancers and other cancers with possible CNS involvement
- Late stage Parkinson's Disease
- Late stage persistent substance dependence
- Ischemic heart disease
- HIV/AIDS
- COPD
- Renal insufficiency
- Diabetes
- Autoimmune or inflammatory disorders
- Chronic non-malignant pain disorders
- Drug effects
- Other acute medical crises

Attachments

INFORMED CONSENT/ASSENT PROCESS/WAIVER

0 unresolved comment(s)

For creating your informed consent attachment(s), please download the most up-to-date version listed in "All Templates" under the APPLICATION LINKS menu on the left, and edit to match your research project.

Additional Resources:

- Informed Consent/Assent Website
- Waiver of Consent vs. Waiver of Signatures
- Sample Repository/Registry/Bank Consent Template

Consent/Assent Tips:

- If you have multiple consent documents, be sure to upload each individually (not all in a combined file).
- If another site is serving as the IRB for the project, attach the form as a “Reliance Consent Form” so the document will not receive a UK IRB approval stamp; the reviewing IRB will need to stamp the consent forms.
- Changes to consent documents (e.g., informed consent form, assent form, cover letter, etc...) should be reflected in a 'tracked changes' version and uploaded separately with the Document Type "Highlighted Changes".
- It is very important that only the documents you wish to have approved by the IRB are attached; DELETE OUTDATED FILES -- previously *approved* versions will still be available in Protocol History.
- Attachments that are assigned a Document Type to which an IRB approval stamp applies will be considered the version(s) to be used for enrolling subjects once IRB approval has been issued.
  Document Types that do NOT get an IRB approval stamp are:
  - "Highlighted Changes",
  - "Phone Script", and
  - "Reliance Consent Form",
  - "Sponsor's Sample Consent Form".

How to Get the Section Check Mark

1. You must:

   a) provide a response in the text box below describing how investigators will obtain consent/assent, and
   b) check the box for at least one of the consent items and/or check mark one of the waivers

2. If applicable attach each corresponding document(s) **as a read-only PDF**.
3. If you no longer need a consent document approved (e.g., closed to enrollment), or, the consent document submitted does not need a stamp for enrolling subjects (e.g., umbrella study, or sub-study), only select "Stamped Consent Doc(s) Not Needed".
4. After making your selection(s) be sure to scroll to the bottom of this section and SAVE your work!

Check All That Apply

- ☐ Informed Consent Form (and/or Parental Permission Form and/or translated short form)
- ☐ Assent Form
- ☐ Cover Letter (for survey/questionnaire research)
- ☐ Phone Script
- ☐ Informed Consent/HIPAA Combined Form
- ☐ Debriefing and/or Permission to Use Data Form
- ☐ Reliance Consent Form
- ☐ Sponsor's sample consent form for Dept. of Health and Human Services (DHHS)-approved protocol
- ☑ Stamped Consent Doc(s) Not Needed

Attachments

Informed Consent Process:

Using active voice, describe how investigators will obtain consent/assent. Include:

- the circumstances under which consent will be sought and obtained
- the timing of the consent process (including any waiting period between providing information and obtaining consent)

- who will seek consent
- how you will minimize the possibility of coercion or undue influence
- the method used for documenting consent
- if applicable, who is authorized to provide permission or consent on behalf of the subject
- if applicable, specific instruments or techniques to assess and confirm potential subjects' understanding of the information

Note: all individuals authorized to obtain informed consent should be designated as such in the E-IRB "Study Personnel" section of this application.

Special considerations may include:

- Obtaining consent/assent for special populations such as children, prisoners, or people with impaired decisional capacity
- *Research Involving Emancipated Individuals*
  If you plan to enroll some or all prospective subjects as emancipated, consult with UK legal counsel **prior to submitting this application to the IRB**. Include research legal counsel's recommendations in the "Additional Information" section as a separate document.
- *Research Involving Non-English Speaking Subjects*
  For information on inclusion of non-English speaking subjects, or subjects from a foreign culture, see IRB Application Instructions for Recruiting Non-English Speaking Participants or Participants from a Foreign Culture.
- *Research Repositories*
  If the purpose of this submission is to establish a research repository describe the informed consent process. For guidance regarding consent issues, process approaches, and sample language see the Sample Repository/Registry/Bank Consent Template.

Trained research staff will obtain sober, written informed consent prior to participation in the screening process (using the Screening Consent form). An investigator or study coordinator will obtain sober, written study consent prior to research participation (with the Main Study Consent form). Participants will be required to have a negative alcohol breathalyzer test prior to signing consent and not be stumbling, nodding or appearing intoxicated. Volunteers who have a positive breathalyzer test or appear intoxicated will be asked to return at a later time when they are sober. Volunteers must be fluent in English and are required to take a literacy test to determine reading level. Volunteers will meet with the investigator, physician or the study coordinator on an outpatient basis prior to admission in order to review all experimental procedures and allow the volunteer to ask any questions regarding the protocol prior to signing the study Informed Consent form. There is no time limit on this process. The investigator will also inform the volunteer that this is not a treatment program and that signing the consent form does not obligate them to participate. Each volunteer will receive a copy of the signed consent forms.

Participants may also be consented via Zoom. All consenting procedures will be identical to an in-person consent, except the PI will be present via Zoom (instead of the same room). The participant will be screened by in-person research staff (e.g., participants provided photo ID, negative breathalyzer samples and protocol-appropriate urine samples; staff confirmed participants were not intoxicated). Research staff will provide the consent form to the participant, which will be verified on camera by the PI. This process allows for a thorough discussion and exchange of information with the participant, a method to ensure the participant's identity, and documentation of the consent itself.
Subjects may ask study personnel questions about the study or make complaints at any time. All staff will be aware to contact Drs. Babalonis, Lofwall or Walsh about any subject concern or complaint as it arises. Phone numbers for the study PI, as well as the Office of Research Integrity are included in the consent form. It is expected that providing a phone number and contact information for the PI may offer a safe, confidential and reliable channel for participants to express problems, concerns or questions and obtain study information.

☐ Request for Waiver of Informed Consent Process

If you are requesting IRB approval to waive the requirement for the informed consent process, or to alter some or all of the elements of informed consent, complete, Section 1 and Section 2 below.

Note: The IRB does not approve waiver or alteration of the consent process for greater than minimal risk research, except for planned emergency/acute care research as provided under FDA regulations. Contact ORI for regulations that apply to single emergency use waiver or acute care research waiver (859-257-9428).

SECTION 1.

Check the appropriate item:

☐ I am requesting a waiver of the requirement for the informed consent process.

☐ I am requesting an alteration of the informed consent process.

If you checked the box for this item, describe which elements of consent will be altered and/or omitted, and justify the alteration.

SECTION 2.

Explain how each condition applies to your research.

a) The research involves no more than minimal risk to the subject.

b) The rights and welfare of subjects will not be adversely affected.

c) The research could not practicably be carried out without the requested waiver or alteration.

d) Whenever possible, the subjects or legally authorized representatives will be provided with additional pertinent information after they have participated in the study.

☐ Request for Waiver of Signatures

If you are requesting IRB approval to waive the requirement for signatures on informed consent forms, **your research activities must fit into one of three regulatory options**:

1. The only record linking the participant and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality (e.g., a study that involves participants who use illegal drugs).
2. The research presents no more than minimal risk to the participant and involves no procedures for which written consent is normally required outside of the research context (e.g., a cover letter on a survey, or a phone script).
3. The participant (or legally authorized representative) is a member of a distinct cultural group or community in which signing forms is not the norm, the research presents no more than minimal risk to the subject, and there is an appropriate alternative mechanism for documenting that informed consent was obtained.

Select the option below that best fits your study.

*If the IRB approves a waiver of signatures, participants must still be provided oral or written information about the study. To ensure you include required elements in your consent document, use the **Cover Letter Template** as a guide. There is an English and a Spanish version.*

○ **Option 1**

Describe how your study meets these criteria:

a) The only record linking the participant and the research would be the consent document:

b) The principal risk would be potential harm resulting from a breach of confidentiality (i.e., a study that involves subjects who use illegal drugs).

Under this option, each participant (or legally authorized representative) must be asked whether (s)he wants to sign a consent document; if the participant agrees to sign a consent document, only an IRB approved version should be used.

○ **Option 2**

Describe how your study meets these criteria:

a) The research presents no more than minimal risk to the participant:

b) Involves no procedures for which written consent is normally required outside of the research context (i.e. a cover letter on a survey, or a phone script):

○ **Option 3**

Describe how your study meets these criteria:

a) The subject (or legally authorized representative) is a member of a distinct cultural group or community in which signing forms is not the norm.

b) The research presents no more than minimal risk to the subject.

c) There is an appropriate alternative mechanism for documenting that informed consent was obtained.

RESEARCH DESCRIPTION

0 unresolved comment(s)

You may attach a sponsor's protocol pages in the "Additional Information" section and refer to them where necessary in the Research Description. However, each prompt that applies to your study should contain at least a summary paragraph.

Pro Tips:

- **Save your work often to avoid losing data.**
- **Use one of the attachment buttons in this section or under the Additional Information section to include supplemental information with your application. During the document upload process, you will be able to provide a brief description of the attachment.**

Background

Include a brief review of existing literature in the area of your research. You should identify gaps in knowledge that should be addressed and explain how your research will address those gaps or contribute to existing knowledge in this area. For interventional research, search PubMed and ClinicalTrials.gov for duplicative ongoing and completed trials with same condition and intervention(s).

Drugged driving is a public health crisis; in the past decade, the number of U.S. traffic fatalities involving at least one driver testing positive for a prescription or illicit drug has risen sharply: 12% in 2005 to 21% in 2015. Further, 10 million American adults reported driving while intoxicated on illicit drugs in the past year (SAMHSA, 2014).

Marijuana is the most widely used "illicit" drug, with 22.2 million current users in the United States (SAMHSA, 2014; Crime, 2016). The U.S. National Highway Traffic Safety Administration reported 8.6% of drivers tested positive for marijuana in 2007, while 12.6% tested positive in 2013–2014 (Berning, 2015). Several epidemiological studies indicate that marijuana involvement produces an approximately 2-fold increase in fatal accident culpability (Asbridge, Hayden, & Cartwright, 2012; Compton RP, 2015; Li, Brady, & Chen, 2013). However, other studies have found no link between marijuana use and driving accidents after controlling for several factors that independently contribute to crash risk (e.g., age, driving experience, presence of alcohol) (Elvik, 2013; Romano, Torres-Saavedra, Voas, & Lacey, 2014; Schulze H, 2012).

Human laboratory studies have reported that smoked marijuana (1.74% – 3.95% THC; 2.9 – 6.7% ad lib availability) produces impairment, specifically increases in lateral position variation (i.e., weaving within the lane) (Papafotiou et al., 2005; Ramaekers et al., 2000; Robbe, 1998; Ronen et al., 2008). However, other studies, utilizing a similar dose range (1.77% - 3.95% THC), have reported no changes in lateral control or other measures of impairment (Anderson et al., 2010; Downey et al., 2013; Lenne et al., 2010; Liguori et al., 1998; Ronen et al., 2010). Further, a common finding across nearly all studies is that marijuana administration produces decreases in speed and increases in distance between vehicles – behavior typically associated with cautious driving and the opposite of the effects seen after administration of impairing doses of alcohol (i.e., increased speed, less distance between vehicles) (Bondallaz et al., 2016; Hartman et al., 2015; Lenne et al., 2010; Papafotiou et al., 2005; Ramaekers et al., 2000; Robbe, 1998).

However, to date, all doses of marijuana tested have contained relatively low THC concentrations (1.74% - 6.7% THC), compared to marijuana that is currently being used for recreational and medicinal purposes. Legal medical and recreational marijuana generally contain very high concentrations of THC, often 20% THC and greater (and up to 80-90% THC in liquid/wax formulations). There are also several popular medical marijuana strains that contain high concentrations of CBD (10% CBD) alone or in combination with THC (Kolikonda et al., 2016) for which there is no data on driving or other performance variables.

The proposed study will employ sophisticated driving simulator methodology to characterize the impairing effects of several strains of marijuana in a tightly controlled laboratory setting. The outcomes selected have been guided by the consensus recommendations from the International Council on Alcohol, Drugs & Traffic Safety (ICADTS) (International Council on Alcohol, 2007) for behavioral outcomes in drugged driving studies and will include lateral control measures (which appear to be most sensitive to marijuana effects), reaction times, steering responses, and obstacle avoidance strategies.

Objectives

List your research objectives. Please include a summary of intended research objectives in the box below.

The primary aim of this project is to enroll healthy occasional marijuana smokers as outpatients to examine the effects of vaporized marijuana strains containing 1) high concentrations of THC (30 mg THC), 2) moderate concentrations of THC + CBD (15 mg THC + 7.5 mg CBD), and 3) moderate concentration of THC (15 mg THC), in comparison to placebo marijuana (negative control) and an alcohol dose known to produce driving impairment (positive control), on simulated driving performance. Secondary aims include examining the abuse liability, cognitive/psychomotor performance, and physiological effects of the dose conditions; sex differences will also be explored.

Study Design

Describe and explain the study design (e.g., observational, secondary analysis, single/double blind, parallel, crossover, deception, etc.).

- *Clinical Research*: Indicate whether subjects will be randomized and whether subjects will receive any placebo.

- *Community-Based Participatory Research*: If you are conducting community-based participatory research (CBPR), describe strategies for involvement of community members in the design and implementation of the study, and dissemination of results from the study.
- *Qualitative research*: Indicate ranges where flexibility is needed, if a fixed interview transcript is not available, describe interview topics including the most sensitive potential questions.
- *Research Repositories*: If the purpose of this submission is to establish a Research Repository (bank, registry) and the material you plan to collect is already available from a commercial supplier, clinical lab, or established IRB approved research repository, provide scientific justification for establishing an additional repository collecting duplicate material. Describe the repository design and operating procedures. For relevant information to include, see the UK Research Biospecimen Bank Guidance or the UK Research Registry Guidance.

This outpatient study will be conducted at the Straus Behavioral Science Research Facility and will last approximately 2-4 weeks per participant. This study will employ a within subject, randomized, double-blind, double-dummy, placebo-controlled crossover design to examine acute marijuana effects on driving performance and a variety of subjective and observer-rated measures.

Due to the double-dummy design of this study, both vaporized marijuana and a cocktail will administered during each session. The vaporized dose will contain an active dose of marijuana or placebo. Cocktails will be comprised of an oral solution containing alcohol (0.8 g/kg, mixed with juice) or placebo (a very small amount of alcohol to mask the placebo). Active marijuana and active alcohol doses will not be administered in combination.

Healthy volunteers will participate in a total of 5 experimental sessions. During each session, the doses will be administered under double-blind conditions, and data will be collected for approximately 8 hours post-dose. Each session is designed to collect an array of multi-dimensional data, including subjective effect questionnaires of positive and negative mood, observer ratings, physiological measures, driving simulator performance and cognitive tasks (see below under Outpatient Research Procedures for further detail).

Attachments

Attach Type	File Name
StudyDesign	Screening Packet.pdf

Subject Recruitment Methods & Advertising

Describe how the study team will identify and recruit subjects. Please consider the following items and provide additional information as needed so that the IRB can follow each step of the recruitment process.

- How will the study team identify potential participants?
- Who will first contact the potential subjects, and how?
- Will you use advertisements? If so, how will you distribute those?
- How and where will the research team meet with potential participants?
- If applicable, describe proposed outreach programs for recruiting women, minorities, or disparate populations.
- How you will minimize undue influence in recruitment?
- Attach copies of all recruiting and advertising materials (emails, verbal scripts, flyers, posts, messages, etc.).

For additional information on recruiting and advertising:

- IRB Application Instructions - Advertisements
- PI Guide to Identification and Recruitment of Human Subjects for Research

Volunteers are recruited primarily through regular newspaper ads, local flyers posted in public areas (e.g., bars, marketplaces), internet postings (including Craigslist.com and ResearchMatch.com) and by word-of-mouth. Flyers and advertisements have our telephone number listed on them, so volunteers typically make initial contact with us by phone. We will also access the UK CCTS Participant Self-Referral Database and will contact individuals who have expressed interest in marijuana-related studies. When calling, a volunteer will speak with one of our trained research staff, all of whom have completed human subjects protection training (web-based CITI and HIPAA-compliance modules). If a volunteer self-discloses information that makes them potentially eligible for the study, he/she will be invited to come in for a screening appointment. Screening is completed by one of our research assistants/research nurses/investigators at the Robert Straus Behavioral Research Facility and/or the UK CCTS. Study investigators may interact with volunteers in any of these settings and appropriate cautions are in place to ensure privacy during the intake process.
We plan to advertise with a PR-approved flyer (attached). We are also requesting permission to use a Facebook page (see attached screenshot) to communicate with participants and to advertise our study.

Attachments

Attach Type	File Name
Advertising	Ad Protocol 43636 APPROVED[1].pdf
Advertising	Facebook account.pdf
Advertising	43636 Ads - July 2019.pdf
Advertising	43636 ads.pdf
Advertising	Cannabis Ad (f) PR STAMPED.pdf
Advertising	Cannabis Ad (f).pdf
Advertising	MJ & Driving Cards - PR APPROVED.pdf
Advertising	MJ & Driving Cards - CLEAN COPY.pdf
Advertising	MJ & Driving Digital Ads - PR APPROVED.pdf

Advertising	MJ & Driving Digital Ads - CLEAN COPY.pdf
Advertising	MJ & Driving Flyers - Final 6.1 - PR APPROVED.pdf
Advertising	MJ & Driving Flyers - Final 6.1 - CLEAN COPY.pdf

Research Procedures

Describe how the research will be conducted.

- What experience will study participants have?
- What will study participants be expected to do?
- How long will the study last?
- Outline the schedule and timing of study procedures.
- Provide visit-by-visit listing of all procedures that will take place.
- Identify all procedures that will be carried out with each group of participants.
- Describe deception and debrief procedures if deception is involved.

Differentiate between procedures that involve standard/routine clinical care and those that will be performed specifically for this research project. List medications that are explicitly forbidden or permitted during study participation.

Screening procedures: Our team of investigators will review all phone screen information and determine whether the caller meets initial screening criteria (e.g., within age limits, reports appropriate drug use history, no current major medical/psychiatric problems). Many volunteers are screened out through this review process (for example, because they reveal a chronic health condition that is exclusionary). The screening process includes at least two separate visits with study staff. This is to ensure that participants are not physically dependent on opiates, alcohol or other sedative/hypnotics and not frequently using other drugs of abuse (e.g., cocaine). Thus, on at least two separate visits, participants will have a breathalyzer and urine drug test. If a volunteer provides a positive alcohol breath sample or urine sample testing positive for a drug of abuse aside from marijuana/THC, we will require that the individual provide subsequent negative breath and urine samples in the absence of signs and symptoms of alcohol/sedative/opioid withdrawal before we will consider study enrollment. As our screening process typically occurs over two or three visits, there are multiple opportunities to collect breath and urine samples. Participants are required to provide at least one urine sample testing negative for all drugs (except THC) during screening and again on each session day. We will test women's urine samples for pregnancy (e.g., urine hCG) during screening and prior to each session. Women testing positive will not be enrolled and will be referred to their primary health care provide or a local women's health clinic for treatment.

All volunteers receive medical and psychiatric screening and examination prior to study participation, including: 1) history and physical examination by a physician, 2) Beck Depression Inventory (screens for depression), 3) Symptom Checklist-90 (general psychiatric symptom inventory), 4) electrocardiogram, 5) laboratory testing (complete blood count with differential, complete metabolic panel, urinalysis with microscopic evaluation, urine drug testing, and urine pregnancy test for females), 6) literacy assessment and 7) evaluation of drug and alcohol use histories. Only those in good medical and psychiatric health, as determined by the study physician, are allowed to participate. Once a person meets inclusion/exclusion criteria, they will be permitted to begin participation in experimental study sessions.

General Methods: Participants will complete one to three training sessions to familiarize them to the driving simulator, the vaporizer procedure (using placebo marijuana), and the various computer tasks to insure that they are comfortable with the equipment and tasks prior to data collection. To familiarize participants with the smoking procedure, placebo marijuana will be administered; participants will be told that the vaporized dose is placebo. After this training is complete, the experimental sessions will be initiated.

Participants will complete a total of 5 experimental sessions. During each session, a battery of assessments will be conducted prior to (as a baseline evaluation) and at regular intervals 8 hours post marijuana dose. These assessments will include an array of subjective, cognitive and psychomotor tasks, driving simulator performance tasks and physiological assessments. The presentation of these assessments is based on the time-active curves for the drugs being tested. On session days, participants will arrive at the laboratory at approximately 9:00 am and will be scheduled to discharge at approximately 6:00 pm (total participation time will be approximately 9 hours).
The content and flow of experimental sessions are designed to capture the time-action curves for the test agents at the selected doses (peak subjective effects of high potency marijuana ˜ 15 mins – 3 hrs (Haney et al., 2016; Hunault et al., 2014; Ramaekers et al., 2006) alcohol (0.8 g/kg) ˜ 15 min – 3 hrs (Kirkpatrick & de Wit, 2013)). The oral alcohol solution will be administered 15 minutes prior to smoked marijuana; however, only one agent will be active (i.e., active alcohol + placebo marijuana; active marijuana + placebo drink). Participants will vaporize marijuana (approx. 166 mg total weight). Driving simulation will be tested at six time points during each test session at baseline, 15 min and 1, 2, 4, and 6 hr post-marijuana dose. This will allow us to examine the driving ability 1) immediately after smoking (15 min), 2) during peak subjective ratings of feeling high (15 mins-2 hrs),(Hunault et al., 2014; Ramaekers et al., 2006) and 3) after subjective intoxication has subsided, but while sedation is expected to remain elevated (6 hrs).(Hunault et al., 2014)

Participants are required 1) to successfully complete a field sobriety test, 2) have a BAC = 0.02, and 3) report no acute intoxication in order to be discharged from the session. Free round-trip transportation will be provided for subject safety (e.g., taxi). Participants are not permitted to transport themselves home.

Study Drug
All drug doses will be stored at the UK Robert Straus Research Facility under secure conditions specially equipped for Schedule I drug storage. Doses will be blinded by the University of Kentucky (UK) Investigational Pharmacy licensed pharmacists (Drs. Seth Larkin, Thomas Lyman). Marijuana will be obtained through the NIDA drug supply. Each vaporized dose will contain approximately 166 mg of plant material. Research Triangle Institute (RTI) will provide chemical analysis reports of marijuana cannabinoid concentrations with each lot of marijuana, which will be reviewed by the PI for consistency. A Volcano brand vaporizer will be used to deliver the doses. This model has been used in several studies (e.g., Spindle et al., 2018; JAMA) and is more efficient delivery system than a marijuana cigarette (drug is lost through combustion and side stream smoke; a vaporizer is a closed system that eliminates these

concerns). Alcohol doses (USP-grade ethanol, juice mixer) and placebo drinks (juice with 1% alcohol) will be prepared by the pharmacists.

Randomized orders will be generated by the statistician. All dosing will be double-blind; however, sealed dose orders will be available on-site and at the pharmacy in the event of an emergency. The drug formulation plans for these studies will be reviewed by the FDA before study initiation. The IND will be submitted after we obtain IRB approval.

Dose Selection
The doses of vaporized marijuana were selected as representative recreational and medicinal marijuana strains that are currently legally available in dispensaries across the U.S.(360, 2017; Sevigny, Pacula, & Heaton, 2014) Strains with 1) high THC/trace CBD, 2) high THC/moderate amounts of CBD are used for medicinal and recreational use (2:1 ratio), and 3) moderate amounts of THC alone (trace CBD) are all used for both medical and recreational purposes. (Lankenau et al., 2016; MA, 2014; Ko, Bober, Mindra, & Moreau, 2016; Kolikonda et al., 2016; Maa & Figi, 2014; 360, 2017; Belendiuk, Babson, Vandrey, & Bonn-Miller, 2015; Freeman & Winstock, 2015; Sevigny et al., 2014).

These doses will provide information regarding the effects of 1) a high dose of THC alone (approximately 30 mg vaporized THC), 2) a moderate dose of THC with CBD (approximately 15 mg THC + 7.5 mg CBD), and 3) moderate dose of THC (approximately 15 mg THC) allowing assessment of a two-fold dose range of THC compared to placebo marijuana (0 mg THC, 0 mg CBD) and will provide some information about the effects of THC combined with CBD. Comparator conditions of doses of CBD alone, or assessments of THC/CBD interactions will not be included in this small-scale exploratory study. The risk of lung infection from vaporized marijuana is stated in the consent form.

The oral solution (e.g., ~16 oz. drink [450 mL/70 kg]) will contain alcohol (0.8 g/kg) or placebo. Placebo is comprised of juice with a very small amount of alcohol [~3mL or approx. 1% alcohol] floated on top of the drink which produces a scent of alcohol, but does not increase breath alcohol levels. Female participants will receive an alcohol dose that is 15% less than the dose administered to men. This allows for comparable breath alcohol concentrations in men and women (as it helps account for differences in body fat and body water). The alcohol solution will be split into three aliquots contained in an opaque covered cup with a straw. Participants will be asked to complete the alcohol solution in 15 minutes (e.g., approx. 5 minutes per aliquot). The active alcohol solution will produce a breath alcohol level of approximately 0.08 within approximately half hour of administration (Kirkpatrick & de Wit, 2013).

Outpatient Methods
For each experimental session, participants will arrive at the laboratory in the morning having abstained from alcohol for 24 hrs, cigarettes and caffeine for 8 hrs, and having fasted (water permitted, no food) since waking. Session will be conducted if urine samples test negative for drugs of abuse (aside from THC) and pregnancy in females; breath samples must test negative (0.000 BAC) for alcohol and cigarette/marijuana smoking abstinence will be confirmed (below approximately 15 PPM CO). After CO is confirmed to be below the cut-off, cigarette smoking and coffee (with standardized caffeine content) will be permitted 1 hr before dosing and after session (we have previously used similar models for marijuana and alcohol studies. A standardized breakfast will be provided approximately 1 hr prior to dose administration.

We have developed driving scenario courses with comparable variables and construct characteristics for use in repeated testing designs. These driving scenarios are approximately 10 minutes in length and include various highway and city driving courses. We are familiar with the consensus recommendations from the International Council on Alcohol, Drugs & Traffic Safety's (ICADTS) for behavioral outcomes in drugged driving studies and will focus on those outcomes most commonly evaluated in driving simulator studies, for example, lateral position variability (i.e., a marker of lane deviation and tactical measures (deceleration maneuvering in response to and obstacle or yellow light). However, other variables will be explored.

Data will be collected for approximately 8 hours post-dose (e.g., relative to marijuana administration) and we expect total session participation time will be approximately 9 hours. A field sobriety test will be completed in the presence of an investigator or senior staff member before participants will be released to go home. If the participant exhibits signs of impairment, they will be retained at the laboratory and re-assessed every 20 minutes (and paid a rate of $10/hr for this extra time). In our experience, the effects of marijuana are minimal at 8 hours post-dose and breath alcohol levels should be 0.00 – 0.02 at this time. Participants will not be permitted to transport themselves home under any circumstance. We will provide transportation (for example: taxi, Uber, similar car service). Alternatively, a participant can arrange for a friend/family member to provide transportation if they choose. We will also advise participants not to use drugs or alcohol on the day of session (either prior to or after the session has been completed) and not to drive a car or operate machinery for the remainder of the day. We have successfully administered smoked marijuana and alcohol on an outpatient basis using similar methods (Protocols #15-0976-F3R, #14-0769-F3R, #11-0100-F6A).

Sessions in which active drug doses are administered will be followed by at least one wash-out day prior to the next session (e.g., minimum of 48 hours between doses).

Urine will be collected prior to each session and will be tested for drugs of abuse. Participants must provide a sample that is negative for all drugs of abuse (except THC) prior to each session. Women's samples will also be tested for pregnancy prior to each session to insure that pregnant women do not continue study participation. Pregnant women will be referred to drug abuse treatment and appropriate prenatal care services.

Two to four weeks after study completion, we will schedule a follow-up visit with each participant to determine his/her health status and drug and alcohol use.

Attachments

Data Collection & Research Materials

In this section, please provide the following:

- Describe all sources or methods for obtaining research materials about or from living individuals (such as specimens, records, surveys, interviews, participant observation, etc.), and explain why this information is needed to conduct the study.
- For each source or method described, please list or attach all data to be collected (such as genetic information, interview scripts, survey tools, data collection forms for existing data, etc.).
- If you will conduct a record or chart review, list the beginning and end dates of the records you will view.

Outcome measures for this study will include physiological measures (such as heart rate, blood pressure, oxygen saturation, respiratory rate, and body temperature), performance on subject-rated questionnaires (such as visual analog questionnaires, opiate adjective ratings, Addiction Research Center Inventory, street value questionnaire, and Pharmacological Class Questionnaire), observer ratings, psychomotor/cognitive tasks (such as the Digit Symbol Substitution Task, Trails Making Task), ocular assessments (such as the Maddox Wing) and driving simulator tasks.

Attachments

Resources

Describe the availability of the resources and adequacy of the facilities that you will use to perform the research. Such resources may include:

- Staffing and personnel, in terms of availability, number, expertise, and experience;
- Computer or other technological resources, mobile or otherwise, required or created during the conduct of the research;
- Psychological, social, or medical services, including equipment needed to protect subjects, medical monitoring, ancillary care, or counseling or social support services that may be required because of research participation;
- Resources for communication with subjects, such as language translation/interpretation services.

The outpatient screening will occur at Straus Behavioral Research Facility on Angliana Avenue and the CCTS outpatient unit. The outpatient sessions will occur at the Straus Behavioral Research Facility. Dr. Lofwall is the primary medically responsible physician. She is an adult psychiatrist with ACLS certification who has worked extensively with individuals with substance use disorders in a clinical and research setting. Our research group at the Straus Facility are able to provide all the necessary staffing and medical oversight to conduct this study and both have had experience with a similar research population and similar research protocols. Dr. Walsh, Director of the Center on Drug and Alcohol, will help provide oversight for the study and has safely completed numerous studies. Overall, the study team and resources described above are well equipped to protect volunteers and successfully implement, carry out, and complete this study.

Potential Risks & Benefits

Risks

- Describe any potential risks – including physical, psychological, social, legal, ability to re-identify subjects, or other risks. Assess the seriousness and likelihood of each risk.
- Which risks may affect a subject's willingness to participate in the study?
- Describe likely adverse effects of drugs, biologics, devices or procedures participants may encounter while in the study.
- *Qualitative research* - describe ethical issues that could arise while conducting research in the field and strategies you may use to handle those situations.
- Describe any steps to mitigate these risks.

Benefits

- Describe potential direct benefits to study participants – including diagnostic or therapeutic, physical, psychological or emotional, learning benefits. This cannot include incentives or payments.
- State if there are no direct benefits.
- Describe potential benefits to society and/or general knowledge to be gained.

Describe why potential benefits are reasonable in relation to potential risks. If applicable, justify why risks to vulnerable subjects are reasonable to potential benefits.

The primary risks to the study participants are related to the ingestion of the study drugs. All participants will be current marijuana smokers and will be familiar with its effects. Marijuana use will be verified by self-report and by collection of an observed urine sample testing positive for THC. Marijuana is a partial CB1/CB2 agonist that has a high therapeutic index and low risk of acute toxicity (Sachs et al., 2015). Marijuana with high levels of THC (up to 23%) has been safely administered to a similar population in several research studies without complication.(Hunault et al., 2014; Ramaekers et al., 2006) High potency strains (with up to 30%+ THC) (Lankenau et al., 2016) and cannabinoid concentrates (with up to 89-90% THC) (Raber et al., 2015) are legally available in U.S. dispensaries and in several international countries (e.g., Netherlands). Similar strains are also being used for medicinal purposes (and medicinal strains are being diverted for recreational use) (Lankenau et al., 2016) No studies to date have examined high-potency CBD strains; however, high doses of oral CBD have been tested in large-scale clinical trials (including pediatric populations) (Devinsky et al., 2014; Devinsky et al., 2016) and our research group has tested acute oral doses (800 mg – the highest acute dose tested in a healthy population) in

marijuana smokers (Babalonis et al., 2016). Some adverse events have occurred in the clinical trials with seizure patients (e.g., somnolence, small subset of participants experiencing increases in seizure frequency) (Devinsky et al., 2014; Devinsky et al., 2016; Tzadok et al., 2016); however, no serious adverse events have occurred when high dose CBD was administered to marijuana smokers (Babalonis et al, 2016) or in studies with normal, healthy drug-free participants.(Cunha et al., 1980; Dalton et al., 1976; Hollister, 1973; Karniol et al.,1974; Zuardi et al.,1993). Participants reporting adverse events from previous marijuana use (e.g., anxiety, panic) or a history of a condition that would increase the likelihood of an adverse event (e.g., bipolar disorder, asthma) will not be enrolled.

Marijuana produces an array of side effects that are typical of CB1/CB2 agonists, including feeling high/intoxicated, euphoria, increased hunger and thirst, perceptual changes, anxiousness, lightheadedness/ dizziness, performance impairment, drowsiness, orthostatic hypotension, resting increases or decreases in blood pressure, increased heart rate, red/bloodshot eyes, dry mouth, sleepiness, concentration difficulties, faintness, restlessness, confusion, loss of coordination, shakiness, stomach upset, headache, paleness, flushing, sweating, slurred speech, fatigue (Cooper & Haney, 2009, 2010; Haney et al., 2016; Hart et al., 2002; Lile et al., 2010). All of the participants will have a history of recreational marijuana use and will be familiar with its effects, decreasing the risk of unanticipated reactions. We have selected inclusion criteria similar to previous well-controlled marijuana studies (conducted by NIDA, our research group, and others) (Cooper & Haney, 2009, 2010; Haney et al., 2016; Hart et al., 2002; Hartman et al., 2015; Lile et al., 2010) and studies that have specifically examined high potency marijuana strains (Hunault et al., 2014; Ramaekers et al., 2006). Our laboratory has experience administering smoked and oral pharmaceutical cannabinoids on both an inpatient (Jicha et al., 2015; Lofwall et al., 2016) and outpatient basis (Babalonis et al., 2016; Haney et al., 2016) and the procedures and doses in this study were selected with care to minimize risk. We have included the risk of lung infection from inhaling marijuana as a potential risk in the consent form - the plant material is stored in a freezer to help minimize risk.

Alcohol side effects include nausea, vomiting, headache, flushing, stimulation, sleepiness, drowsiness, feeling tired, changes in heart rate and blood pressure, changes in motor coordination, reaction time, vision, balance, hearing and speech.

The simulated driving environment may also produce some side effects in a small percentage of people (e.g., simulator sickness). These side effects include headache, nausea, dizziness, motion sickness and vomiting. During training sessions, participants will complete simulated driving tasks; we will not enroll individuals who exhibit signs of significant simulator sickness during training.

The placement of needles in a vein for blood draws during screening may cause pain, soreness, bleeding, bruising, inflammation, thrombosis, infection or fainting. There is also a risk that a participant's Protected Health Information (PHI) or other non-PHI information may be seen by others resulting in a loss of confidentiality that could embarrass them and/or cause them psychological distress. The risk of this happening is low.
The degree of risk to which individual study volunteers are exposed as a consequence of their research participation is low. In contrast, the potential and probable benefits to be derived by society and to public health and safety appear to be considerable. The major benefits of this study are scientific and clinical ones related to the knowledge gained regarding driving after consuming common marijuana strains (and their performance will be compared to their ability to drive after an impairing dose of alcohol). Individual volunteers are expected to benefit personally from the medical and psychiatric evaluations, referrals for medical and psychiatric treatment that are provided whenever appropriate, and the financial payments, which are provided for their research participation. Overall, the risk/benefit ratio appears favorable and the conduct of this research seems well justified.

Available Alternative Opportunities/Treatments

Describe alternative treatments or opportunities that might be available to those who choose not to participate in the study, and which offer the subject equal or greater advantages. If applicable, this should include a discussion of the current standard of care treatment(s).

This is not a treatment study - there are no available alternative treatments.

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Records, Privacy, and Confidentiality

Specify where the data and/or specimens will be stored and how the researcher will ensure the privacy and confidentiality of both. Specify who will have access to the data/specimens and why they need access.

Describe how data will be managed after the study is complete:

- If data/specimens will be maintained, specify whether identifiers will be removed from the maintained information/material.
- If identifiers will not be removed, provide justification for retaining them and describe how you will protect confidentiality.
- If the data/specimens will be destroyed, verify that this will not violate retention policies and will adhere to applicable facility requirements.

If this study will use de-identified data from another source, describe what measures will be taken to ensure that subject identifiers are not given to the investigator.

If applicable, describe procedures for sharing data/specimens with collaborators not affiliated with UK.

For additional considerations:
Return of Research Results or Incidental Research Findings
HIPAA policies
FERPA policies

Procedures for Transfer agreements
Information regarding multi-site studies
NIH Genomic Data Sharing (GDS) Policy
Digital Data

Sources of research material obtained from our volunteers during screening and study participation include: blood and urine specimens, expired breath samples for alcohol, electrocardiogram, self-reported information gathered from the volunteer about their and their families psychiatry and medical history, demographic information, volunteer self-report and study staff observation of drug effects, vital signs (oxygen saturation, temperature, blood pressure, pulse), and other physiologic indices (e.g., pupil diameter). All sources of research material will be obtained in a HIPAA compliant manner and are collected specifically for the proposed study by trained study staff. The principal investigator and medical team will have access to private health information about volunteers so that determination of study eligibility can be determined. All data with personal health information is kept in a locked file cabinet separate from other volunteer data without identifiable private health information. Prior medical records may be obtained with volunteer consent if there is any question about the volunteers' health history. Each participant will sign a form that details the HIPAA-compliant manner in which research material is collected.
Identifying information will be stored in a separate locked area from all other data and codes that could link the two. Incidental materials containing subject identifiers will be shredded or incinerated. Identification and access of identifying data/specimens will be available only to study investigators when it is detrimental to subject safety or the conduct of the research protocol. For example, if a subject has an adverse event we will want to obtain a quantitative drug screen to identify whether there may have been illicit drug use while in the study versus a true adverse even related to the study procedures. In addition, a Certificate of Confidentiality will be obtained.
All participants are carefully screened (history and physical exam with physician, routine labs such as CBC, urinalysis, ECG and psychiatric assessment) to exclude those with potential increased risk of adverse effects. Those at increased risk include a history of heart disease, history of seizure or head injury associated with more than a brief loss of consciousness, hypertension, psychosis, and history of adverse reactions to the study drugs. During sessions participants remain under careful observation and are monitored continuously by on-site research staff. Vital signs, including ongoing monitoring of blood pressure and heart rate, will be collected at regular intervals throughout the dosing period. Clinical staff (e.g., M.D. or R.N.) will be available for management of medical issues. Trained personnel draw blood according to routine hospital procedures under sterile conditions that should significantly reduce the risk of any adverse effects from blood draws. In addition, we have substantial experience testing cannabinoids and alcohol in human subjects under a variety of dosing conditions. Female participants will be given pregnancy tests prior to each experimental session to ensure that we do not administer drugs or alcohol to a pregnant woman.

To protect confidentiality, all research subjects are identified by a subject identification code (Subject ID) consisting of their initials and sequentially assigned subject numbers on all forms and data files, and not by their names. Actual subject names and corresponding subject IDs are kept in a locked master file separate from the actual data collected during the study. All personal and experimental information is kept locked and is accessible only to key personnel involved in the research.

All volunteer information and data are confidential and never released to anyone outside of the project purview without the volunteer's written authorization. The identity of participants is never revealed in research reports. All intake documentation that contains PHI is handled separately from the actual data collected during the study. For instance, written records with PHI will be stored in a separate, locked area from all other de-identified data and codes linking the two will be kept under lock and key. Electronic data with PHI (e.g., blood and urine test results) are stored in the University of Kentucky's medical database that has limited medical personnel access, is password protected, and monitored for abnormal activity. Incidental materials containing subject identifiers will be shredded or incinerated.

UK IRB policies state that IRB-related research records must be retained for a minimum of 6 years after study closure. Do you confirm that you will retain all IRB-related records for a minimum of 6 years after study closure?

◉ Yes ○ No

Payment

Describe the incentives (monetary or other) being offered to subjects for their participation. If monetary compensation is offered, indicate the amount and describe the terms and schedule of payment. Please review this guidance for more information on payments to subjects, including restrictions and expectations.

Participants will be paid for each screening visit at the rate of $50 per visit. If only a urinalysis or ECG or vital signs are needed subjects will be paid $15. Volunteers will earn $50 for each training session (approximately 4 hours in length) and $25 for a 2- to 4-week follow-up appointment. Volunteers will earn $80 base pay for each session in which they participate. They will also be paid $5 per drive if the course is completed within the specified time limit (e.g., approx. 9 minutes). We anticipate completing 6 driving scenarios per session, so participants have the opportunity to earn up to an additional $30/session. This money will be given to participants along with their base pay. Participants will be paid a study bonus of $80/session if they complete each of the 5 sessions. If the volunteer chooses to leave before completing the study, they will not receive the completion bonus. However, if the participant is discharged early due to unrelated medical issues or investigator decision related to safety (e.g., an adverse reaction to the study drug), they will be paid the completion bonus for the duration of their participation. If participants complete all of the 6 sessions, they will receive a total payment of $800 (not including screening, practice sessions, bonus pay for drive completion times, or follow-up payments).

Costs to Subjects

Include a list of services and/or tests that will not be paid for by the sponsor and/or the study (e.g., MRI, HIV). Keep in mind that a subject will not know what is "standard" – and thus not covered by the sponsor/study – unless you tell them.

There are no costs to volunteers who participate in this study.

Data and Safety Monitoring

The IRB requires review and approval of data and safety monitoring plans for greater than minimal risk research or NIH-funded/FDA-regulated clinical investigations.

- If you are conducting greater than minimal risk research, or your clinical investigation is NIH-funded, describe your Data and Safety Monitoring Plan (DSMP). Click here for additional guidance on developing a Data and Safety Monitoring Plan.
- If this is a non-sponsored investigator-initiated protocol considered greater than minimal risk research, and if you are planning on using a Data and Safety Monitoring Board (DSMB) as part of your DSMP, click here for additional guidance for information to include with your IRB application.

Data Safety and Monitoring Plan: Data will be collected using a computerized data collection and management system wherever possible. This system automates the collection of data, which ensures the accuracy and completeness of data collection. The data are stored in a unique file on the hard drive of the computer and are printed after all the tasks are completed. In all instances, the data files do not contain the name of the subject; but instead, a unique eight-digit number identifies each subject. A computer file linking the unique number with the subject's name will be kept on a stand-alone, password-protected encrypted computer. All data requiring hand entry (e.g., urinalysis results) will be double entered by two separate staff members and comparison macros conducted to ensure accuracy. Data files for experimental tasks and physiological measures from each experimental session will be manipulated and combined into a single electronic spreadsheet for each subject by the statistician. Data for all volunteers will then be combined into a single electronic spreadsheet and separated by experimental measure for statistical analysis. The primary outcome measures will include driving performance on key measures (e.g., SDLP, brake latency, reaction time, collisions). Secondary outcomes will include observer ratings, safety outcomes (side effects and physiological measures) and cognitive/psychomotor performance; sex differences will be explored. Data will be analyzed using LMM for repeated measures designs along with other statistical analyses. The alpha level will be set at 5%. As noted above, wherever possible, data are collected using an automated computer system, which increases the accuracy and completeness of data collection and ensures the validity and integrity of the data. The initial data manipulation described above will be conducted twice and compared. All analyses are conducted by our statistician (Mr. Paul Nuzzo). The quality of manipulated data and data analyses will be monitored by random inspection by the PI and/or Co-Investigators.

Volunteers will be approximately 24 men and women of varying race/ethnicity, aged 21-50, who are in good physical health, who report occasional marijuana use (approx. 1 occasion in the past 3 months; less than or equal to 3 days/week),8,14,29 occasional alcohol use and endorse at least one instance of lifetime alcohol intoxication, no current moderate to severe alcohol use disorder, no current prescription drug use or physiological drug dependence on a drug requiring medical detoxification (e.g., alcohol, benzodiazepines). All participants will be current weekly drivers with a history of approx. 2 years of driving.14 All volunteers must provide informed consent to participate. This sample will be recruited from the local community and will participate as outpatients at the Robert Straus Behavioral Science Research Facility. The Principal Investigator, Shanna Babalonis, Ph.D., along with co-investigators (Dr. Sharon Walsh) and medically-responsible physician (Dr. Michelle Lofwall) will be responsible for monitoring the safety and effective implementation of this project, executing the DSMP, and complying with the reporting requirements.

Potential volunteers will provide information regarding their drug use history and undergo an extensive physical and psychiatric health screening to determine their eligibility and safety of their participation. Potential volunteers must report no recent recreational drug use (aside from marijuana) and must present with urine samples negative for drugs (aside from THC) during screening. Any potential subject with a history of clinically significant physical disease, current serious physical disease (e.g., impaired cardiovascular functioning, histories of seizure, head trauma) or current or past histories of psychiatric disorder will be excluded from research participation. Females must be using an effective form of birth control in order to participate and must not be pregnant. Methods for monitoring adverse events (AEs) will include observations by the medical and research staff, spontaneous report by the volunteers, regular measurement of physiological indices and subjective drug effects questionnaires. Volunteers will not receive study drug if they have any signs or symptoms that may contraindicate its administration (e.g., heart rate and blood pressure outside of predetermined range for a prolonged period, development of serious side effects). All AEs occurring during the course of the study will be collected, documented and reported to the PI and Co-Investigators. The occurrence of AEs will be assessed for the duration of participation and during follow-up visits at 2-4 weeks or as long as needed. Each week a study investigator will review the AE forms from the previous week for events that were reported as new or continuing. The study investigators will follow all AEs to the point of a satisfactory resolution. Volunteers may be withdrawn from the study if the medically responsible investigator (Dr. Lofwall) determines it is the best decision in order to protect the safety of the subject. All AEs will be assessed to determine if they meet criteria for a serious adverse event (SAE). Serious Adverse Events, as defined by the FDA, will be systematically evaluated for the duration of participation and during the follow-up visits at 2 and 4 weeks following study completion (or longer as needed until resolution). Any SAE, whether or not related to the study drug, will be reported to the IRB, NIH and the FDA. The initial SAE report will be followed by submission of a completed SAE report to all three institutions. In the event that a volunteer either withdraws from the study or the investigator decides to discontinue a volunteer due to an SAE, the volunteer will have appropriate follow-up medical monitoring. Monitoring will continue until the problem requiring hospitalization has resolved or stabilized with no further change expected, is clearly unrelated to the study drugs or results in death.

Data and Safety Monitoring Board (DSMB): NIH requires the establishment of Data and Safety Monitoring Boards (DSMBs) for 1) multi-site clinical trials involving interventions that entail potential risk to the volunteers and 2) for most Phase III clinical trials. This project meets neither of these definitions and, therefore, it is not likely that a DSMB will be required, but will be established if requested.

Future Use and Sharing of Material (e.g., Data/Specimens/Information)

If the material collected for this study will be used by members of the research team or shared with other researchers for future studies, please address the following:

- list the biological specimens and/or information that will be kept
- briefly describe the types, categories and/or purposes of the future research
- describe any risks of the additional use
- describe privacy/confidentiality protections that will be put into place
- describe the period of time specimens/information may be used
- describe procedures for sharing specimens/information with secondary researchers
- describe the process for, and limitations to, withdrawal of specimens/data

There is a possibility that data/tissue/specimens/blood collected during the screening process may be shared with other investigators in the future. If this is the case, the data/tissue/specimen/blood will not contain identifying information unless the individual provides consent/authorization or an Institutional Review Board (IRB) approves the research. Language to this effect is included in IRB-approved Screening consent form. Information or samples collected during the main study will NOT be shared for future research studies, even if identifiable information is removed. Language to this effect is included in the IRB-approved Main Study consent form. See Confidentiality section of Research Description for additional information about confidentiality/privacy protections.

Are you recruiting or expect to enroll **Non-English Speaking Subjects or Subjects from a Foreign Culture**? (does not include short form use for incidentally encountered non-English subjects)

○ Yes ◉ No

Non-English Speaking Subjects or Subjects from a Foreign Culture

Recruitment and Consent:

Describe how information about the study will be communicated to potential subjects appropriate for their culture, and if necessary, how new information about the research may be relayed to subjects during the study.
When recruiting Non-English-speaking subjects, provide a consent document in the subject's primary language. After saving this section, attach both the English and translated consent documents in the "Informed Consent" section.

Cultural and Language Consultants:

The PI is required to identify someone who is willing to serve as the cultural consultant to the IRB.

- This person should be familiar with the culture of the subject population and/or be able to verify that translated documents are the equivalent of the English version of documents submitted.
- The consultant should not be involved with the study or have any interest in its IRB approval.
- Please include the name, address, telephone number, and email of the person who agrees to be the cultural consultant for your study.
- ORI staff will facilitate the review process with your consultant. Please do not ask them to review your protocol separately.

For more details, see the IRB Application Instructions on Research Involving Non-English Speaking Subjects or Subjects from a Foreign Culture.

Local Requirements:

If you will conduct research at an international location, identify and describe:

- relevant local regulations
- data privacy regulations
- applicable laws
- ethics review requirements for human subject protection

Please provide links or sources where possible. If the project has been or will be reviewed by a local ethics review board, attach a copy in the "Additional Information/Materials" section. You may also consult the current edition of the International Compilation of Human Research Standards

Does your study involve **HIV/AIDS research and/or screening for other reportable diseases (e.g., Hepatitis C, etc…)**?
○ Yes ◉ No

HIV/AIDS Research

If you have questions about what constitutes a reportable disease and/or condition in the state of Kentucky, see ORI's summary sheet: "Reporting Requirements for Diseases and Conditions in Kentucky" [PDF].

HIV/AIDS Research: There are additional IRB requirements for designing and implementing the research and for obtaining informed consent. Describe additional safeguards to minimize risk to subjects in the space provided below.

For additional information, visit the online IRB Survival Handbook to download a copy of the "Medical IRB's requirements for Protection of Human Subjects in Research Involving HIV Testing" [D65.0000] [PDF], and visit the Office for Human Research Protections web site for statements on AIDS research, or contact the Office of Research Integrity at 859-257-9428.

PI-Sponsored FDA-Regulated Research

Is this an investigator-initiated study that:

1) involves testing a Nonsignificant Risk (NSR) Device, or
2) is being conducted under an investigator-held Investigational New Drug (IND) or Investigational Device Exemption (IDE)?
◉ Yes ○ No

PI-Sponsored FDA-Regulated Research

If the answer above is yes, then the investigator assumes the regulatory responsibilities of both the investigator and sponsor. The Office of Research Integrity provides a summary list of sponsor IND regulatory requirements for drug trials [PDF], IDE regulatory requirements for SR device trials [PDF], and abbreviated regulatory requirements for NSR device trials [PDF]. For detailed descriptions see FDA Responsibilities for Device Study Sponsors or FDA Responsibilities for IND Drug Study Sponsor-Investigators.

- Describe the experience/knowledge/training (if any) of the investigator serving as a sponsor (e.g., previously held an IND/IDE); and
- Indicate if any sponsor obligations have been transferred to a commercial sponsor, contract research organization (CRO), contract monitor, or other entity (provide details or attach FDA 1571).

This study will be covered by an IND (141,123); see attached. Dr. Babalonis also received a DEA Schedule I drug license (RB0545763); see attached.

The PI, Dr. Shanna Babalonis, will obtain the IND. Dr. Babalonis will work under the guidance and mentorship of Dr. Sharon Walsh (who has been conducting FDA-regulated research for 20+ years). Through her work with Dr. Walsh, Dr. Babalonis has gained extensive experience submitting INDs, amendments, is familiar with reporting requirements for adverse events, annual progress reporting requirements and record keeping requirements. She is also familiar with Good Clinical Practice guidelines and has participated in numerous related trainings over the years. She has assisted with training and managing a multi-disciplinary staff on regulatory affairs, confidentiality issues, reporting requirements, data management, data quality assurance, data storage, and human subjects' protections. Dr. Babalonis has completed the FDA investigational drug sponsor-investigator training available through the ORI.

IRB policy requires mandatory training for all investigators who are also FDA-regulated sponsors (see Sponsor-Investigator FAQs). A sponsor-investigator must complete the applicable Office of Research Integrity web based training, (drug or device) before final IRB approval is granted.

Has the sponsor-investigator completed the mandatory PI-sponsor training prior to this submission?
◉ Yes ○ No

If the sponsor-investigator has completed equivalent sponsor-investigator training, submit documentation of the content for the IRB's consideration.

Attachments

Attach Type	File Name
SponsorInvTraining	SBabalonis DEA License Exp July 2020.pdf
SponsorInvTraining	SBabalonis Certificate.pdf
SponsorInvTraining	IND 141123.pdf

HIPAA

0 unresolved comment(s)

Is HIPAA applicable? ◉ Yes ○ No

(Visit ORI's Health Insurance Portability and Accountability Act (HIPAA) web page to determine if your research falls under the HIPAA Privacy Regulation.)

If yes, check below all that apply and attach the applicable document(s):

☐ HIPAA De-identification Certification Form

☐ HIPAA Waiver of Authorization

Attachments

STUDY DRUG INFORMATION

0 unresolved comment(s)

The term drug may include:

- FDA approved drugs,
- unapproved use of approved drugs,
- investigational drugs or biologics,
- other compounds or products intended to affect structure or function of the body, and/or
- complementary and alternative medicine products such as dietary supplements, substances generally recognized as safe (GRAS) when used to diagnose, cure mitigate, treat or prevent disease, or clinical studies of e-cigarettes examining a potential therapeutic purpose.

Does this protocol involve a drug including an FDA approved drug; unapproved use of an FDA approved drug; and/or an investigational drug?

◉ Yes ○ No

If yes, complete the questions below. Additional study drug guidance.

LIST EACH DRUG INVOLVED IN STUDY IN THE SPACE BELOW

Drug Name:

Marijuana, alcohol

Note: Inpatient studies are required by Hospital Policy to utilize Investigational Drug Service (IDS) pharmacies (Oncology or Non-Oncology). Use of IDS is highly recommended, but optional for outpatient studies. Outpatient studies not using IDS services are subject to periodic inspection by the IDS for compliance with drug accountability good clinical practices.

Indicate where study drug(s) will be housed and managed:

☑ Investigational Drug Service (IDS) UK Hospital

Other Location:

Marijuana will be stored at the Robert Straus Research Facility in our secure Schedule I drug storage area. Alcohol will be stored at the IDS.

Is the study being conducted under a valid Investigational New Drug (IND) application?

◉ Yes ○ No

If Yes, list IND #(s) and complete the following:

141123

IND Submitted/Held by:

Sponsor: ☐	Held By:		
Investigator: ☑	Held By:	Shanna Babalonis, Ph.D.	
Other: ☐	Held By:		

☐ Checkmark if the study is being conducted under FDA's Expanded Access Program (e.g., Treatment IND) or if this is an Individual Patient Expanded Access IND (FDA Form 3926).

FDA's Expanded Access Program Information for Individual Patient Expanded Access INDs, and attach the following:

- FDA Form 3926;
- FDA expanded access approval or correspondence;
- Confirmation of agreement from manufacturer or entity authorized to provide access to the product.

For guidance and reporting requirements at the conclusion of treatment see the Expanded Access SOP.

Complete and attach the required Study Drug Form picking "Study Drug Form" for the document type. Any applicable drug documentation (e.g., Investigator Brochure; approved labeling; publication; FDA correspondence, etc.) should be attached using "Other Drug Documentation" for the document type.

Attachments

Attach Type	File Name
Study Drug Form	Study Drug Form - Updated September 3 2019.pdf

KEY INFORMATION FOR

MEDICAL & ELIGIBILITY SCREENING:

MARIJUANA AND ALCOHOL EFFECTS ON SIMULATED DRIVING PERFORMANCE

You are being invited to take part in medical and screening procedures to determine if you are eligible to take part in a research study about the effects of marijuana and alcohol on simulated driving performance.

WHAT IS THE PURPOSE, PROCEDURES, AND DURATION OF THIS STUDY?

The purpose of this screening is to conduct an interview, screening questionnaires and a medical examination that will help us find out if you qualify for study participation. There are approximately 3 screening visits that last about 4 hours each.

The purpose of the main study is to learn more about the influence of marijuana and alcohol on simulated driving performance. If you qualify, you will be invited to participate in a study where you will receive marijuana and alcohol under supervision. If you participate and pass the screening, the study will be described further in another consent form.

WHAT ARE REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

You may choose to volunteer for this study to earn extra money. However, there are no other direct benefits to you for taking part in this study. Your willingness to take part may help us understand how alcohol and marijuana affect driving performance.

WHAT ARE REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You may not have the time necessary to screen for the study or participate (participation requires at least one full 9 hr day per week) – please let us know if this is a concern.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of this study is Shanna Babalonis, Ph.D. of the University of Kentucky, Department of Behavioral Science and Center on Drug and Alcohol Research. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study her contact information is: **(859) 257-1881.**

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact staff in the University of Kentucky (UK) Office of Research Integrity (ORI) between the business hours of 8am and 5pm EST, Monday-Friday at 859-257-9428 or toll free at 1-866-400-9428.

DETAILED CONSENT:

ARE THERE REASONS WHY YOU WOULD NOT QUALIFY FOR THIS STUDY?

If you are under the age of 21 years of age or older than 50 years of age, you will not be allowed to take part in this screening. If you are seeking treatment for drug abuse, you should not take part in this study; please tell us now and we will help you find treatment.

WHERE IS THE STUDY GOING TO TAKE PLACE AND HOW LONG WILL IT LAST?

The research procedures will be conducted at the Robert Straus Behavioral Research Facility and/or the Center for Clinical and Translational Science (CCTS), a research unit located in the University of Kentucky Hospital. The intake interview and physical examination should last about 3 to 4 hours. The entire screening will require more than one visit. The number of screening visits will range from approximately 1-4 visits.

WHAT WILL YOU BE ASKED TO DO?

If you agree to be screened, we will ask you to take part in an interview/complete screening materials to see if you qualify for this study. You can stop the visit anytime you want. Completion of the interview/screening materials will take approximately 3-4 hrs per visit. You will be asked about the following:

- Your past and present personal life and problems
- Your alcohol and drug use
- Your mood and behavior
- Your health and family health (including medical and psychiatric history)
- Legal history and problems
- Living conditions
- Driving status and experience
- You will be asked to give urine and breath samples when a staff member is watching. These samples will be tested for drugs and alcohol.
- The names, addresses and phone numbers of people (such as a parent, spouse or close friend) that we can contact in case of an emergency or if we cannot find you to conduct a future interview.
- You will also have a medical exam, psychiatric evaluation and complete questionnaires
- You will have a physical exam, an ECG (electrodes applied to your chest) and a small amount of blood and urine taken for testing.
- Women will also be required to have a pregnancy test.
- We will also ask your permission to review your prescription medication history (KASPER report) and medical records from health care visits.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

There is a risk that discussing some of the topics covered in the interview might be upsetting. As noted above, you are free to stop the interview at any time. There is a risk that someone other than the study team could see your personal information; we will try very hard to make sure that no one gets your personal information.

During the screening process, we will draw your blood and conduct an ECG. There are risks related to drawing blood. These include soreness, bruising, pain, infection, possible fainting and bleeding. It is possible that we may have to try more than once to draw blood. An ECG is painless; however, the electrodes may feel cold when first applied. In rare cases, some people may develop a rash or irritation where the patches were placed.

In addition to the risks listed above, you may experience a previously unknown risk or side effect.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

You will not get any personal benefit from taking part in this screening. The only benefit that you may receive is a free medical exam.

WHAT WILL IT COST YOU TO PARTICIPATE?

The screening procedures will be provided at no cost to you.

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

We will make every effort to keep confidential all research records that identify you to the extent allowed by law. Your information will be combined with information from other people taking part in the study. When we write about the study to share it with other researchers, we will write about the combined information we have gathered. You will not be personally identified in these written materials. We may publish the results of this study; however, we will keep your name and other identifying information private. We will collect your social security number; this is required in order for you to participate.

We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is. Your name will be kept separate from the information that you give, and these two things will be stored in different places under lock and key. Information collected electronically will be stored on password-protected computers.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below. You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

You should know that there are some circumstances in which we may have to show your information to other people. For example, the law may require us to show your information to a court or to tell authorities if you report information about a child being abused or if you pose a danger to yourself or someone else. The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under certain circumstances including: abuse or neglect, harm to self or others, or diagnosis of certain communicable diseases (including but not limited to, hepatitis C, HIV, or tuberculosis), which will be reported to the State Health Department along with your full name as required by law.

Officials of the Food and Drug Administration, National Institutes of Health, and the University of Kentucky may look at or copy pertinent portions of records that identify you.

CAN YOU CHOOSE TO WITHDRAW FROM THE STUDY EARLY?

You can choose to leave the study at any time. You will not be treated differently if you decide to stop taking part in the study.

The investigators conducting the study may need to remove you from the study. This may occur for a number of reasons. You may be removed from the study if:

- you are not able to follow the directions,
- they find that your participation in the study is more risk than benefit to you, or
- the agency paying for the study chooses to stop the study early for a number of scientific reasons.

If you stop the study because of side effects from the medication or another health-related reason, we will follow-up with you by telephone or request that you come visit us so we can see how you are doing.

ARE YOU PARTICIPATING, OR CAN YOU PARTICIPATE, IN ANOTHER RESEARCH STUDY AT THE SAME TIME AS PARTICIPATING IN THIS ONE?

You **may not** take part in this study if you are currently involved in another research study. It is important to let the investigator know if you are in another research study. You should discuss this with the investigator before you agree to participate in another research study while you are in this study.

WHAT HAPPENS IF YOU GET HURT OR SICK DURING THE STUDY?

If you believe you are hurt or if you get sick because of something that is done during the study, you should call Michelle Lofwall, M.D. **(859) 323-9321**. Dr. Lofwall will determine what type of treatment, if any, is best for you at that time.

It is important for you to understand that the University of Kentucky does not have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. That cost will be your responsibility. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study. The medical costs related to your care and treatment because of research related harm will be your responsibility.

You do not give up your legal rights by signing this form.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?

You will receive payment for your participation. You will receive $50 for each screening visit. If your screening is completed but you need to come back in only to give a urine sample for additional drug testing or for an ECG, you will receive $15 each time.

WHAT IF NEW INFORMATION IS LEARNED DURING THE STUDY THAT MIGHT AFFECT YOUR DECISION TO PARTICIPATE?

You will be informed if the investigators learn new information that could change your mind about staying in the study. You may be asked to sign a new informed consent form if the information is provided to you after you have joined the study.

WHAT ELSE DO YOU NEED TO KNOW?

There is a possibility that data/tissue/specimens/blood collected from you may be shared with other investigators in the future. If that is the case, the data/tissue/specimen/blood will not contain information that can identify you unless you give your consent/authorization or the UK Institutional Review Board (IRB) approves the research. The IRB is a committee that reviews ethical issues, according to federal, state and local regulations on research with human subjects, to make sure the study complies with these before approval of a research study is issued.

This study is funded by the National Institute of Health/National Institute on Drug Abuse.

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

POTENTIAL FUTURE CONTACT

Do you give your permission to be contacted in the future by staff of the UK Center on Drug and Alcohol Research regarding your willingness to participate in future research studies?

□ **Yes** **No** _____**Initials**

AUTHORIZATION TO USE OR DISCLOSE YOUR IDENTIFIABLE HEALTH INFORMATION

The privacy law, HIPAA (Health Insurance Portability and Accountability Act), requires researchers to protect your health information. The following sections of the form describe how researchers may use your health information.

Your health information that may be accessed, used and/or released includes:

Demographic information, social security number, results of physical exams, blood tests, and urine test results.

The Researchers may use and share your health information with:

- The University of Kentucky's Institutional Review Board/Office of Research Integrity;
- Law enforcement agencies (only when required by law)
- University of Kentucky representatives;
- UK Hospital
- The National Institutes of Health and/or its divisions
- The Investigational Drug Service (IDS) at the University of Kentucky
- Food and Drug Administration
- Center for Clinical and Translational Science (CCTS)

If you are a woman and you become pregnant anytime during the study or within 30 days after discharging from the study, you must inform Dr. Lofwall or Dr. Babalonis – they must then report the outcome of your pregnancy to the Sponsor (and/or the FDA).

The researchers agree to only share your health information with the people listed in this document.

Should your health information be released to anyone that is not regulated by the privacy law, your health information may be shared with others without your permission; however, the use of your health information would still be regulated by applicable federal and state laws.

You may not be allowed to participate in the research study if you do not sign this form. If you decide not to sign this form, it will not affect your:

- Current or future healthcare at the University of Kentucky;
- Current or future payments to the University of Kentucky;
- Ability to enroll in any health plans (if applicable); or
- Eligibility for benefits (if applicable).

After signing the form, you can change your mind and NOT let the researcher(s) collect or release your health information (revoke the Authorization). If you revoke the authorization:

- You will send a written letter to Dr. Babalonis to inform her of your decision. Her address is:
  Shanna Babalonis, Ph.D.
  845 Angliana Avenue
  Lexington, KY, 40508
- Researchers may use and release your health information **already** collected for this research study.
- Your protected health information may still be used and released should you have a bad reaction (adverse event).
- You may not be allowed to participate in the study.

The use and sharing of your information has no time limit.

If you have not already received a copy of the Privacy Notice, you may request one. If you have any questions about your privacy rights, you should contact the University of Kentucky's Privacy Officer between the business hours of 8am and 5pm EST, Monday-Friday at (859) 323-1184.

INFORMED CONSENT SIGNATURE PAGE

You are a participant or are authorized to act on behalf of the participant. This consent includes the following:

- **Key Information Page**
- **Detailed Consent**

You will receive a copy of this consent form after it has been signed.

_____	_____
Signature of research participant	**Date**
_____	
Printed name of research participant	
_____	_____
Printed name of person obtaining informed consent/ HIPAA authorization	Date
_____	
Signature of Principal Investigator or Sub/Co-Investigator	