Document Coversheet

Study Title: Re-entry XR-NTX for Rural Individuals With Opioid Use Disorder

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	11/7/2022 (Protocol); 12/1/2021 (ICF)
NCT Number:	NCT03447743
IRB Number	43830
Coversheet created:	2/23/2023

PROTOCOL TYPE (VERSION 4)

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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.

EXPEDITED CERTIFICATION

0 unresolved comment(s)

To Be Completed Only If Protocol is to Receive Expedited Review

Applicability

A. Research activities that (1) present no more than *minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.
B. The categories in this list apply regardless of the age of subjects, except as noted.
C. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
D. The expedited review procedure may not be used for classified research involving human subjects.
E. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

**"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. 45 CFR 46.102(i)*

Check the appropriate categories that apply to your research project:

☑ Study was originally approved by the full IRB at a convened meeting.

☐ 1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

A. Research on drugs for which an investigational new drug application is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
B. Research on medical devices for which (i) an investigational device exemption application is not required*; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.**

* Study must meet one of the IDE Exempt categories listed on the Device Form Attachment.
** An approved Device used in research according to its approved labeling is considered Exempt from IDE requirements.
NOTE: Select Category 1 for compassionate use medical device applications or individual patient expanded access investigational drug applications for which FDA has waived the requirement for full review.

☐ 2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

A. From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
B. From other adults and children* considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

NOTE: Intravenous (IV), Port, Central, or any other lines are NOT eligible under this category even if the research involves "minimal risk".

*In Kentucky, "child/children" refers to all individuals less than 18 years of age unless the individual(s) is/are legally emancipated. (See Informed Consent SOP for discussion of "Emancipated Individuals" under Kentucky state law.) Individuals less than 18 years of age who are not emancipated meet the federal definition for "child" (e.g., DHHS, FDA, and U.S. Department of Education). Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." If conducting research outside the state of Kentucky, you are responsible for complying with applicable state law.

☐ 3) Prospective collection of biological specimens for research purposes by noninvasive means. Examples:

A. Hair and nail clippings in a nondisfiguring manner;
B. Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
C. Permanent teeth if routine patient care indicates a need for extraction;
D. Excreta and external secretions (including sweat);
E. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;
F. placenta removed at delivery;
G. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
H. Supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
I. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
J. Sputum collected after saline mist nebulization.

☐ 4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples:

A. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;
B. Weighing or testing sensory acuity;
C. Magnetic resonance imaging;
D. electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;
E. moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

☐ 5) Research involving materials (data, documents, records, or specimens) that have been or will be collected solely for non-research purposes (such as medical treatment or diagnosis) as well as research involving existing information or specimens that were previously collected for research purposes, provided they were not collected for the currently proposed research. (Note: Some research in this category may qualify for Exempt review. This listing refers only to research that is not exempt.)
(Note: If submission includes materials previously collected for either non-research or research purposes in a protocol for which IRB approval expired, you may check Category 5. However, a separate category must also be selected for prospective collection of data/specimens obtained solely for research purposes)

☐ 6) Collection of data from voice, video, digital, or image recordings made for research purposes.

☐ 7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. This listing refers only to research that is not exempt.)

CONTINUATION REVIEW/FINAL REVIEW

0 unresolved comment(s)

In accordance with federal regulations and/or local policies, the IRB conducts periodic review of all currently approved projects. If you need your IRB approval to continue and you do not complete and submit the required materials in a timely manner, IRB approval will expire at the end of your current approval period.

If you have any questions, please contact the Office of Research Integrity at 859-257-9428.

To initiate your continuation review (CR)/annual administrative review (AAR), or properly close your study, complete this section and update/correct all other sections of your IRB application as applicable. ***IMPORTANT* Before leaving this page to update other sections of your application, be sure to SAVE this section first.**

1. Status of the Research

Check the statement(s) that best describe(s) the current status of your research:

- ☐ No subjects have enrolled to date.
- ☐ Recruitment and/or enrollment of new subjects or review of records/specimens continue.
- ☐ Study is closed to enrollment, but subjects still receive research-related interventions (e.g., treatment, blood draws).
- ☐ Study enrollment is permanently closed; subjects have completed all research-related interventions; and the study remains active only for long-term follow-up of subjects (see Tool Tip above for info on long-term follow-up of subjects).*
- ☐ Research has progressed to the point that it involves 1) Data analysis, including analysis of identifiable private information or identifiable biospecimens; and/or 2) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.*
- ☑ The remaining research activities are limited only to data analysis. There is access to records or specimens either directly or through codes or links to the data.*
- ☐ The remaining research activities are limited only to data analysis. There is no subject/record/specimen identifying codes or links to the data; the researcher or research team cannot readily ascertain the subject's identity.*
- ☐ All study activities are complete. IRB approval can be inactivated.

*Possibility that review will move from Full to Expedited.

2. If subjects have been enrolled within the last year, and the IRB approved a consent/assent form for your study, attach one copy of the entire signed consent/assent form/HIPAA form for the last TWO subjects enrolled.

Attachments

Attach Type	File Name
CR_EntireConsent	Screening Consent PD.pdf
CR_EntireConsent	Trial Consent PD.pdf
CR_EntireConsent	Screening Consent AS.pdf
CR_EntireConsent	Trial Consent AS.pdf

3. Informed Consent

If the study is **open to subject enrollment, please go to the Informed Consent section of the E-IRB Application and verify attachment(s) include:**

- One clean copy in PDF (without the IRB Approval stamp) of the currently approved consent/assent document(s), or,
- If requesting changes to the consent/assent document(s), submit one copy with the changes highlighted (and designate Document Type as "Highlighted"), and one clean copy in PDF (without the changes highlighted).

If the study is **open to subject enrollment and the IRB has waived the requirement to document informed consent, please go to the Informed Consent section of the E-IRB Application and verify attachment(s) include:**

- One clean copy in PDF of the currently approved document used for the informed consent process (e.g., cover letter, phone script), or,
- If requesting changes to the consent/assent document(s), submit one copy with the changes highlighted (and designate Document Type as "Highlighted"), and one clean copy in PDF (without the changes highlighted).

If the study is **closed to subject enrollment, please go to the Informed Consent section of the E-IRB Application and remove Informed Consent Documents designated to get an IRB approval stamp to avoid having them appear valid for enrollment.**

4. Unanticipated Problems Involving Risk to Subjects or Others/Adverse Events Summary & Assessment

Did any **problems/adverse events** occur during the last 12 months?

○ Yes ◉ No

In the space below, provide a written summary of both unanticipated problems* and available information regarding adverse events since the last review (e.g., initial review or annual/continuing review). The amount of detail provided in such a summary will vary depending on the type of research being conducted; in many cases, such a summary could be a brief statement that there have been no unanticipated problems and that adverse events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document, and investigator's brochure (if applicable). **The summary must include the PI's assessment whether the problems/adverse events warrant changes to the protocol, consent process, or risk/benefit ratio.**

Note: It is the IRB's expectation that all unanticipated problems involving risk to subjects or others or related deaths requiring prompt reporting are submitted in the appropriate time frame (See Policy [PDF]). Your response to this Annual/Continuing Review is considered assurance that all prompt reportable problems/adverse events have been submitted for IRB review.

*For multisite studies, the written summary should describe external events determined to be unanticipated problems involving risk to subjects or others.

5. Subject Info To-Date

Our records for the previously approved IRB application indicate the **IRB approved estimate** of subjects to be enrolled (or records/specimens reviewed) is:

84

Enter the number of enrolled subjects (or records/specimens reviewed) that **have not been previously reported** to the IRB

9

Our records for the previously approved IRB application indicate the previous total # of subjects enrolled (or records/specimens reviewed) since activation of the study is:

23

The new total number of subjects enrolled (or records/specimens reviewed) since activation of the study:

32

Please review the Project Info section for the IRB approved estimate of subjects to be enrolled (or records/specimens reviewed). If this new total exceeds your approved estimate of subjects to be enrolled (or records/specimens reviewed), please update the number in the field for Number of Human Subjects in the Project Info section.

6. Data and Safety Monitoring Board (DSMB)/Plan (DSMP)

If your study is monitored by a DSMB or under a DSMP, attach all documentation (i.e. summary report; meeting minutes) representing Data and Safety Monitoring activities that have not been previously reported to the IRB.

Attachments

7. Since the most recent IRB Initial/Continuation Review Approval:

Have there been any **participant complaints** regarding the research?

○ Yes ◉ No

If yes, in the field below, provide a summary describing the complaints.

Have any **subjects withdrawn** from the research voluntarily or by you as the PI for reasons related to safety, welfare, or problems related to the conduct of the research? If a participant does not meet the screening criteria for a study even if they signed a screening consent it is NOT considered a withdrawal.

○ Yes ◉ No

If yes, in the field below, provide a detailed explanation to the withdrawal(s) including if participants were lost to contact.

Has any **new and relevant literature** been published since the last IRB review, especially literature relating to risks associated with the research?

○ Yes ◉ No

If yes, attach a copy of the literature as well as a brief summary of the literature including, if pertinent, the impact of the findings on the protection of human subjects.

Attachments

Have there been any **interim findings?**

○ Yes ◉ No

If yes, attach a copy of **Interim Findings**.

Attachments

Have **subjects experienced any benefits?**

○ Yes ◉ No

If yes, in the field below, provide a description of benefits subjects have experienced.

Have there been any **inspections/audits/quality improvement reviews** of your research protocol resulting in the need for corrective action in order to protect the safety and welfare of subjects?

○ Yes ◉ No

If yes, please attach documentation evidencing the outcome(s) and any corrective action(s) taken as a result.

Attachments

Was an FDA 483 issued as a result of any inspections/audits?

○ Yes ◉ No

If yes, submit documentation using attachment button above.

8. Risk Level:

Our records for the previously approved IRB application show your research is:

Risk Level: **2**

Has something during the course of your research changed the level of risk?

◉ Yes ○ No

If yes, go to the Risk Level section, mark the appropriate risk level, and in the field below, describe why the risk level has changed:

Risk level has been revised to 1. The remaining research activities are limited to data analysis.

9. Funding/Support:

Our records for the **previously approved** IRB application indicate your research is being submitted to, supported by, or conducted in cooperation with the following external or internal agency(ies) or funding program(s):

☑ Grant application pending

- [x] (HHS) Dept. of Health & Human Services
  - [x] (NIH) National Institutes of Health
  - [ ] (CDC) Centers for Disease Control & Prevention
  - [ ] (HRSA) Health Resources and Services Administration
  - [ ] (SAMHSA) Substance Abuse and Mental Health Services Administration
- [ ] (DoJ) Department of Justice or Bureau of Prisons
- [ ] (DoE) Department of Energy
- [ ] (EPA) Environmental Protection Agency
- [ ] Federal Agencies Other Than Those Listed Here
- [ ] Industry (Other than Pharmaceutical Companies)
- [ ] Internal Grant Program w/ proposal
- [ ] Internal Grant Program w/o proposal
- [ ] National Science Foundation
- [ ] Other Institutions of Higher Education
- [ ] Pharmaceutical Company
- [ ] Private Foundation/Association
- [ ] U.S. Department of Education
- [ ] State

Other:

Please **update the Funding/Support section of your IRB application** if needed, including the following attachments if they contain changes not previously reported to the IRB:

- A current copy of your **protocol if you are conducting industry/pharmaceutical research;**
- A current **Investigator Brochure** (submit a copy with all changes underlined).
- A **new or revised grant application** for this project.

Did your project receive extramural funding?

(•) Yes ( ) No

If yes, please review and correct if necessary, the OSPA Account # information under the **Funding/Support section** of your IRB application.

If the project is externally funded, has the sponsor offered any of the research team enrollment incentives or other personal benefit bonuses? (e.g., cash/check, travel reimbursements, gift checks, etc.)

( ) Yes (•) No ( ) N/A

Note: It is University of Kentucky policy that personal benefit bonuses are not allowed. If these conditions change during the course of the study, please notify the IRB.

10. Project Information

Our records for the previously approved IRB application indicate your estimated project end date is:

03/31/2023

If you have a new estimated project end date, please go to the Project Info section and change the date in the field for Anticipated Ending Date of Research Project.

11. Study Personnel

Our records for the previously approved IRB application indicate the following individuals are study personnel on this project (if applicable):

Last Name	First Name
Webster	John
Oser	Carrie
Walsh	Sharon
Winston	Erin

Last Name	First Name
Lofwall	Michelle
Shalash	Sophia
Seaver	Robert
Bush	Heather
Dickson	Megan
Knudsen	Hannah
Engle	Sarah
Pike	Erika
Litton	Elyse
Bailey	Egan
Acree	Tianna
Frost	Kathy
Levi	Mary
Calvert	Joseph
Tillson	Martha
Anderson	Brittany
Williams	Summer
Flores	Katrin
Stamper	Roscoe
Napier	Ellen
Hardin	Vicky
Hopper	Vera
Williams	Allyson
Fugate	Layla
Mitchell	Kathleen
Spicer	Amber
Wells	Shelly
Reynolds	Jennifer
White	Joshua
Sparkman	Deloris
Sizemore	Calvin
White	Tiffany
Mullins	Jenny
McIntosh	Amy

Please review the individuals listed above and update your records as needed in the Study Personnel section of the E-IRB application, being sure that each individual listed has completed or is up-to-date on the mandatory human research protection training [see the policy on Mandatory Human Subject Protection Training FAQs (required every three years)].

12. Progress of the Research

To meet federal requirements the IRB is relying on your RESEARCH DESCRIPTION as a protocol summary and their expectation is that it is up-to-date. If the currently approved protocol (or research description) in your E-IRB application is outdated, please make applicable changes, and describe in the field below any substantive changes and explain why they are essential. If none, insert "N/A" in the text field below. If you are closing your study, you may use the space below to summarize the final status of the research.

N/A

Note: No changes in the research procedures should have occurred without previous IRB review. Approval from the IRB must be obtained before implementing any changes.

Provide a brief **summary** of any **modifications that affect subject safety and/or welfare** approved by the IRB since the last initial or continuation review (If none, insert "N/A" in the text field below.):

N/A

Attach one copy of the most recent progress report sent to the FDA, if available. All PI-sponsored IND/IDE studies are required to submit a copy of the FDA progress report.

Attachments

13. Confidentiality/Security

Review your Research Description section and update the Confidentiality portion, if necessary, to describe measures for security of electronic and physical research records (e.g., informed consent document(s), HIPAA Authorization forms, sensitive or private data).

14. Subject Demographics

Our records for the previously approved IRB application indicate the following categories of subjects and controls are included in your research:

- ☐ 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
- ☐ International Citizens
- ☐ Normal Volunteers
- ☐ Military Personnel and/or DoD Civilian Employees
- ☐ Patients
- ☑ Appalachian Population

Please review the Subject Demographics section of your IRB application for accuracy, and note the following:

If during the course of your research 1) any prisoners have been enrolled, OR 2) subjects have been enrolled that became involuntarily confined/detained in a penal institution that have not been previously reported to the IRB, go to Subject Demographic section in your E-IRB application and mark “prisoners” in the categories of subjects to be included in the study, if it is not already marked.

Note: If either 1 or 2 above apply, and you have received funding from the Department of Health and Human Services (HHS), a Certification Letter should have been submitted to the Office for Human Research Protections (OHRP); prisoners and individuals who

have become involuntarily confined/detained in a penal institution cannot continue participation in the research until OHRP issues approval. If the Certification has not been submitted, contact the Office of Research Integrity.

Based on the **total # of subjects** who have enrolled, complete the subject demographic section below:

Participant Demographics

	Cisgender Man	Cisgender Woman	TGNB/TGE	Unknown/Not Reported
American Indian/Alaskan Native	0	0	0	0
Asian	0	0	0	0
Black or African American	0	0	0	0
Latinx	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0
White	14	5	0	0
American Arab/Middle Eastern/North African	0	0	0	0
Indigenous People Around the World	0	0	0	0
More than One Race	0	0	0	0
Unknown or Not Reported	0	0	0	13

If unknown, please explain why:

Aim 1: Ten (n=10) individuals have completed qualitative interviews and provided demographics. Aim 2: Demographics are collected at baseline (n=9), thus are unknown for participants who do not complete baseline (n=13).

15. Research Sites

Our records for the previously approved IRB application indicate that you are conducting research at the following sites:

UK Sites

- ☐ UK Classroom(s)/Lab(s)
- ☐ UK Clinics in Lexington
- ☐ UK Clinics outside of Lexington
- ☐ UK Healthcare Good Samaritan Hospital
- ☐ UK Hospital

Schools/Education Institutions Schools/Education Institutions

- ☐ Fayette Co. School Systems *
- ☐ Other State/Regional School Systems
- ☐ Institutions of Higher Education (other than UK)

Other Medical Facilities

- ☐ Bluegrass Regional Mental Health Retardation Board
- ☐ Cardinal Hill Hospital
- ☐ Eastern State Hospital
- ☐ Nursing Homes
- ☐ Shriner's Children's Hospital
- ☐ Other Hospitals and Med. Centers

- ☑ Correctional Facilities
- ☐ Home Health Agencies
- ☐ International Sites

Other:

Kentucky River Regional Jail
The Little Flower Clinic-an FWA for Little Flower has been obtained due to NIH funding requirements, and the IAA to reflect that agreement is attached to the application.

If the above listed sites are not accurate, go to the Research Sites section of the E-IRB application to update the facilities at which research procedures have been or will be conducted.

If you are adding a new off-site facility, you may also need to update your E-IRB application Research Description, Research Sites, Informed Consent, and other affected sections as well as any documents which will list the off-site facility. Documents needing updating may include, but not limited to:

- Consent forms (attachment under Informed Consent section)
- Brochures (attachment under Additional Info section)
- Advertisements (attachment under Research Description section) ;
- Letter of support (attachment under Research Sites section)).

Please revise applicable sections and attachments as necessary.

16. Disclosure of Significant Financial Interest

Disclosure of Significant Financial Interest:

Our records for the previously approved IRB application indicate that you, your investigators, and/or key personnel (KP) have a significant financial interest (SFI) related to your/their responsibilities at the University of Kentucky (that requires disclosure per the UK administrative regulation 7:2):

○ Yes ◉ No

If you need to update your records, please go to the PI Contact Information section and/or Details for individuals listed in the Study Personnel section to change your response to the applicable question(s).

17. Supplementals

To ensure the IRB has the most accurate information for your protocol you are expected to re-visit the E-IRB application sections and make corrections or updates as needed. At a minimum you are being asked to review the following sections for accuracy:

STUDY DRUG INFORMATION—Please review for accuracy.
STUDY DEVICE INFORMATION—Please review for accuracy.
RESEARCH ATTRIBUTES—Please review for accuracy.
OTHER REVIEW COMMITTEES -- Please review for accuracy.

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

Re-entry XR-NTX for rural individuals with opioid use disorder

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.

Re-entry XR-NTX

Anticipated Ending Date of Research Project: 3/31/2024

Maximum number of human subjects (or records/specimens to be reviewed) 84

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

PI CONTACT INFORMATION

0 unresolved comment(s)

Principal Investigator (PI) role for E-IRB access
The PI is the individual holding primary responsibility on the research project with the following permissions on the E-IRB application:

1. Read;
2. write/edit;
3. receive communications; and
4. submit to the IRB (IR, CR, MR, Other Review*).

If research is being submitted to or supported by an extramural funding agency such as NIH, a private foundation or a pharmaceutical/manufacturing company, the PI listed on the grant application or the drug protocol must be listed as PI here.

Please fill in any blank fields with the appropriate contact information (gray shaded fields are not editable). Required fields left blank will be highlighted in pink after you click "Save".

To change home and work addresses, go to myUK and update using the Employee Self Service (ESS) portal. If name has changed, the individual with the name change will need to submit a 'Name Change Form' to the Human Resources Benefits Office for entering into SAP. The new name will need to be associated with the individual's Link Blue ID in SAP before the change is reflected in E-IRB. Contact the HR Benefits Office for additional information.

The Principal Investigator's (PI) contact information is filled in automatically based on who logged in to create the application.

If you are not the Principal Investigator, do NOT add yourself as study personnel.
To change the PI contact information on an application in Researcher edit status:

- click "Change Principal Investigator";
- search for the PI's name using the search feature;
- click "Select" by the name of the Principal Investigator, then "Save Contact Information".

  You will automatically be added as study personnel with editing permissions to continue editing the application.

Change Principal Investigator:

First Name:	Christa	Room# & Bldg:	141 Medical Behavioral Science Building
Last Name:	Staton	Speed Sort#:	40536
Middle Name	M.		
Department:	Behavioral Science - 7H150	Dept Code:	7H150
PI's Employee/Student ID#:	00008256	Rank:	Assoicate Professor
PI's Telephone #:	859-312-8245	Degree:	PhD, MSW
PI's e-mail address:	mstaton@uky.edu	PI's FAX Number:	
PI is R.N.	○ Yes ◉ No	HSP Trained:	Yes
		HSP Trained Date:	5/26/2021
		RCR Trained:	Yes

Do you, the PI, have a significant financial interest related to your responsibilities at the University of Kentucky (that requires disclosure per the UK administrative regulation 7:2)?

○ Yes ◉ No

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..) 18 to 99

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

Gender disparities faced by Appalachian individuals call for the critical need for prevention services for this high-risk population. Research indicates that women drug users, in general, are more likely to have injecting intimate partners, and with fewer economic resources to buy drugs, they are more likely to engage in sex exchange to obtain drugs. So, women will be prioritized in this trial. Studies of rural drug users are challenging because recruitment of this high-risk population can be limited by the lack of formal treatment opportunities, travel distances to study sites, and the general protective nature of rural social networks (Friedman, 2003). This study will utilize local rural jails as venues for screening and recruitment of high-risk drug users, followed by targeted prevention efforts in the community post-release. For Aim 1, the study population will include stakeholders (n=10) who are community health/behavioral health providers and community supervision officers. Aim 1 will also include participants (n=20) in focus groups who mirror the pilot trial inclusion/exclusion criteria. The second set of interviews will include key stakeholders who work in community supervision and health care providers (n=15) and individuals who have used opioids and are incarcerated or on community supervision (n=15). For Aim 2, the pilot trial will include participants who are incarcerated at the time of study recruitment or currently on community supervision in Perry County, KY (n=60). Based on pre-screening and medical evaluation, inclusion and exclusion criteria is described below, and summarized in the attached Research Strategy:

Inclusion Criteria
• Meets criteria for opioid use disorder
• Anticipated release date within 30 days
• Opioid free
• Not currently in methadone or buprenorphine trial
• No serious medical or psychiatric condition
• Willingness to enroll in the trial
• Currently has or is willing to obtain Medicaid or other health insurance coverage
Exclusion Criteria
• Positive study pregnancy test
• Abnormal liver function tests (5X upper limits of normal)
• Chronic pain conditions that require opioid therapies
• Untreated medical or psychiatric disorder
• Suicidal ideation
• BMI > 40 Medical evaluation

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:				
Asian:				
Black/African American:		2		
Latinx:				
Native Hawaiian/Pacific Islander:				
White:	32	50		
American Arab/Middle Eastern/North African:				

Indigenous People Around the World:				
More than One Race:				
Unknown or Not Reported:				

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

PRISONERS

0 unresolved comment(s)

SECTION 1.

For studies involving **prisoners** or people at risk of becoming involuntarily detained during the research (e.g., subjects with substance abuse history), respond to the following items. For information on restrictions and regulatory requirements, see ORI's Research Involving Prisoners web page.

For research involving prisoners, the definition of minimal risk refers to the probability and magnitude of **physical** or **psychological** harm that is normally encountered in the daily lives, or in the routine medical, dental or psychological examination of healthy persons.

Select the category below that best represents your research and explain why your research meets the criteria.

Prisoner Categories

- ○ **Category 1: My research involves the study of possible causes, effects, processes of incarceration, and of criminal behavior.** (Processes of incarceration can be interpreted broadly to include substance abuse research, half-way houses, counseling techniques, criminal behavior, etc.)
- ○ **Category 2: My research involves the study of prisons as institutional structures, or of prisoners as incarcerated persons.** (This category is usually used fairly narrowly – i.e., looking at prisoner diet, conditions of prison, etc.)
- ○ **Category 3: My research involves the study of conditions particularly affecting prisoners as a class.** (This category is rarely used – e.g., vaccine trials, research on hepatitis, social and psychological problems such as alcoholism, drug addiction, sexual assaults. Minimal risk studies should not go under this category.)
- ◉ **Category 4: My research involves the study of practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject.** (Rare for research involving placebo or control groups to fall in this category because of the difficulty in justifying improvement of the health or well-being of the subject being given placebo or in a control group.) Note: Contact the Office of Research Integrity at (859) 257-9428 for more information.
- ○ **Epidemiologic Research Involving Prisoners [See also SECTION 3 below]**

Explain the research practices that will be used in this study and how they are intended to improve the health and well-being of the participants:

This study will identify, screen, assess, and provide treatment for high-risk rural individuals with OUD. Study participants will have equal opportunity to be screened for high-risk opioid use and opioid use disorder. Participants will have the opportunity to participate in a thorough medical evaluation including urinalysis, pregnancy testing, LFT, and HIV and HCV pre-test counseling and testing with results provided during the baseline. Based on the research for XR-NTX, it is expected that study participants will benefit from receiving the medication and addiction services to decrease illicit drug use and reduce risk for relapse and overdose during the high-risk period of community re-entry.

SECTION 2.

When an IRB is reviewing a protocol in which a prisoner will be a subject, the IRB must find and document justification that six additional conditions are met. Describe in the space provided how each condition applies to your research.

NOTE: If your study **only** involves epidemiologic research, you may insert "N/A" in each of the text boxes in this section (Section 2). Your response to Section 3 will determine appropriateness for "N/A" answers here.

Condition 1. Advantages acquired through participation in the research, when compared to the prisoners' current situation, are not so

great that they impair their ability to weigh risks.

Describe the possible advantages that can be expected for prisoner participants:

This study has a few advantages for participants. First, study participants will have equal opportunity to be screened for high-risk opioid use and opioid use disorder. Second, participants will have the opportunity to participate in a thorough medical evaluation including urinalysis, pregnancy testing, LFT, and HIV and HCV pre-test counseling and testing with results provided during the baseline. Third, based on the research for XR-NTX, it is expected that study participants will benefit from receiving the medication and addiction services to decrease illicit drug use and reduce risk for relapse and overdose during the high-risk period of community re-entry. Fourth, there will be significant potential benefits to science because the study will provide important information about the feasibility, acceptability, and short term outcomes associated with an effective, life-saving medication for opioid dependence among high-risk individuals in rural areas who otherwise face enormous challenges to accessing treatment. Finally, the project will generate important information related to the feasibility of XR-NTX treatment for rural drug users, providing the formative work needed to advance access to treatment through criminal justice venues which can be tailored to high-risk and underserved populations.

Condition 2. Risks are the same as those that would be accepted by non-prisoners.

Describe the possible risks that can be expected for prisoner participants and justify that they are the same as for non-prisoners:

The procedures to be used by this study will involve conventional social science research and treatment methods that are routine in re-entry XR-NTX studies. The potential risks in this study are mainly related to use of the study medication, which is the same for prisoners and non-prisoners. The potential risks will be discussed with participants during recruitment, screening, and the informed consent process to assist them in making a voluntary decision as to whether they wish to participate in the study protocol. These risks are explained further in the Research Description and Informed Consent forms.

In addition to possible risks associated with the medications, other potential psychological risks are primarily related to being asked questions in the interview that they do not feel comfortable asking. It is possible, that a participant may experience anxiety, emotional distress, or other negative reactions due to the content of the interview questions, HIV/HCV testing procedures, and/or treatment participation. Based on our experiences working with this population, such occurrences are rare.

Condition 3. Procedures for selection are fair to all prisoners and are immune from intervention by prison authorities in prisons; control subjects must be randomly selected.

a) Describe how prisoners will be selected for participation:

Randomly selected inidividuals will be screened to assess recent high-risk opioid use. Face-to-face screening (estimated 10 minutes) will be conducted by the research coordinator. The session will include informed consent and an emphasis on the voluntary nature of participation. Consenting participants will be administered the NIDA-modified ASSIST (NIDA, 2009) to measure high risk opioid use, including injection, prior to entering jail. Participants will be asked about their interest and willingness to engage in XR-NTX treatment, as well as their probation/parole status following release. Participants who screen positive for high-risk opioid use and anticipate leaving the jail on probation or parole to District 11 will then see the study nurse for a medical evaluation to determine study eligibility. Study eligibility includes: 1) not currently pregnant, or have a positive pregnancy test during the study medical screening; 2) opioid free based on urine drug screen; 3) not currently enrolled in a methadone or buprenorphine medication trial; 4) no serious medical or psychiatric condition; 5) normal liver function test; 6) no chronic pain conditions; 7) no evidence of suicidal ideation, 8) body mass index less than 40; and 9) planning to be released from jail within 3 months.

b) Describe what measures will be taken to prevent intervention by prison authorities in the selection process:

Consistent with our current R01 (IRB protocol #12-0372), while jail staff may monitor participant entry and exit into the visitation room for the screening, medical evaluation, and interview process, no jail staff will be present for any study related procedures.

Condition 4. Parole boards cannot take into consideration a prisoner's participation in research. Informed consent must state participation will not impact parole.
Describe what measures are in place to ensure parole boards are not influenced by prisoners' participation in research and how prisoners will be told their participation (or refusal or withdrawal from) will not impact parole:

Based on our current study, we anticipate that most of our participants will be on probation rather than parole. However, confidentiality issues will be stressed during informed consent and will include the description of a federal Certificate of Confidentiality. Participants will also be assured that their screening results, HIV/HCV test results, study participation, and study data will not be made available to any representative of the jail or criminal justice system. Jail officials and administrators will not be informed of participants who participate in the screening, eligibility data, or refusals in order to protect participant confidentiality. Consent form language reflects this emphasis on participant confidentiality.

Condition 5. For studies that require follow-up, provisions are made including consideration for the length of individual sentences; informed consent must reflect provisions for follow-up.
Describe what provisions have been made for follow-up and how this information will be relayed to the prisoner participants:

Follow-up data will be collected with all study participants three months post-release from jail through (1) Medical Management Assessment (MMA), and (2) the 3-month post-release interview. For study participants in both conditions, data will be collected at each monthly visit with the study nurse through the MMA. The MMA will include an assessment of compliance with the medication, potential side effects, and symptoms associated with cravings in the previous 30 days. The MMA will also include a brief overall health assessment. During the MMA, participants will be asked to provide a urine sample for drug testing to ensure opioid abstinence, as well as to document short-term outcomes for the study at 1 month, 2 months, and 3 months post-release. At the 3-month follow-up, baseline measures will be repeated by the research coordinator to assess risk behaviors during the re-entry period, which is consistent with other trials.

Condition 6. Information about the study is presented in a language understandable to prisoners.
Describe what efforts have been made to present information about the study in a language understandable to the prisoner population:

All questions in the required assessments are constructed to be understandable by individuals with an 6th grade education or less. Additionally,

data is collected via a face-to-face interview by the UK research assistants, thus there will be an

individual present to help provide clarification/prompts for any questions not understood by the participant.

SECTION 3. Epidemiologic Research Involving Prisoners
Only complete if applicable:

Effective June 20, 2003, DHHS adopted policy that allows waiver of the requirement for documenting applicability of a category (as found in Section 1 of this form) for certain epidemiologic research involving prisoners. This waiver applies to epidemiologic research on prisoners that presents no more than minimal risk and no more than inconvenience to the prisoner-subjects.

☐ Check this box if your research meets all three criteria listed below, then provide justification in the space provided.

1. I request a waiver for meeting the category conditions under Section 1 of this form.
2. My research involves epidemiologic research intended to describe the prevalence/incidence of a disease by identifying all cases, or to study potential risk factor associations for a disease; **and**
3. Prisoners are not the sole focus of my research.

Justify how the research presents no more than minimal risk and no more than inconvenience to the subjects:

SECTION 4. Prisoners are not the targeted population
Only complete if applicable:

Although prisoners may not be the target population for your research, a subject could become a prisoner during the course of the study (particularly if studying a subject population at high-risk of incarceration).

Note: If you did not receive IRB approval for involvement of prisoners, and a subject becomes a prisoner during the study, **all research activities involving the now-incarcerated participant must cease** until IRB approval has been issued for their continuation in the research. If you need IRB approval for a prisoner subject to continue participation in your research, select and complete the applicable category from Section 1, complete section 2 and this section, then submit for IRB review.

In special circumstances where it is in the best interest of the subject to remain in the research study while incarcerated, the IRB Chairperson may determine that the subject may continue to participate in the research prior to satisfying the requirements of Subpart C. However, subsequent IRB review and approval of this completed form is required.

☐ Prisoners are not a target population for my research, but a subject became a prisoner during the study and I am seeking IRB approval so the subject can continue participation in the research.

Explain the importance of continuing to intervene, interact, or collect identifiable private information during the participant's incarceration:

SECTION 5. Kentucky (KY) Department of Corrections (DoC) Approval

Review the following conditions and determine whether any apply to your study:

- active recruitment of participants from a correctional facility (prison, jail, or community corrections institution);
- active recruitment of individuals under community supervision from a state probation and parole office.

If any of the above conditions apply to your research, refer to the Kentucky Department of Corrections Policy and Procedures, Management Information and Research (Chapter 5) for information about submitting a proposal for DoC approval of research including the DoC approved Research Consent and Research Agreement (5.1.G.1).

If your research involves a certificate of confidentiality or the Department of Corrections is directly involved in the study as a sponsor (or otherwise), contact David Kinsella, Legal Counsel, at David.Kinsella@uky.edu, or 859-323-1161, for additional information.

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 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.

Aim 1: Potential participants will be read the interview script and will be asked to verbally consent to completing the interview. A waiver of documented informed consent has been requested, because the consent document would be the only link between the research activities and the participant (Option 1) and the main risk would be related to a breach of confidentiality. Participants will be offered the opportunity to sign a stamped consent form if they would prefer.

Aim 2: Potential participants who are interested in the study will be asked to participate in the screening session at the jail with the UK research coordinator (See Research Procedures). Potential participants will be provided with informed consent prior to the screening session. As part of the informed consent process, potential participants will be assured that: (a) Neither participation nor refusal to participate in a protocol will affect their legal parole status (if applicable); (b) No individual or identifiable data collected as part of a study protocol will be made available to any criminal justice authority including jail, parole, or community mandated treatment; and (c) If potential participants do NOT wish to participate, their parole or other legal status will not be affected. Potential participants who choose NOT to participate in the study protocol will not be identified in their records, and non-participation will NOT become a matter of official record in any file. For the focus groups, the consent procedure will only cover the focus group. Focus groups will be audio recorded unless anyone objects. For the pilot trial, informed consent procedures will cover participation in the screening session, medical evaluation, HIV/HCV testing procedures, baseline interview, medication trial, and follow-up interviews so that participants are fully aware of all possible study procedures and possible risks before making a decision about entering the study. A medication guide for Vivitrol will also be given to each participant. Due to the sensitive nature of some of the questions asked in the interviews, confidentiality issues will be stressed during informed consent which will include a description of a federal Certificate of Confidentiality which provides an additional layer of human subject protection. Participants will also be assured that their screening results, study participation, and study data will not be made available to any representative of the criminal justice system. The research coordinator will keep detailed records on the number of interested participants who participate in the screening session and the number of refusals. Screening data will be examined as part of the implementation phase to examine characteristics of participants who enter the study compared to those who are not eligible. Because of the short time frame between baseline and follow-up interview (3 months), consent procedures will not be repeated since no new procedures will be introduced.
The Kentucky Department of Corrections (DOC) requires us to provide the DOC with the study title and participant name of individuals under their supervision, including inmates, parolees, or individuals likely to be incarcerated by the DOC.

**Due to COVID-19 restrictions, we are requesting a waiver of documented informed consent (described in detail in the Informed Consent page) for the Screening consent only. Research staff will still review the Screening consent in detail with potential participants over the phone and there will be a section added to the IRB-approved Screening consent document for staff to verify that they reviewed the consent with the participant, answered any questions, that the participant agreed to participate in the study, and the participant's name. The research activities covered in the Screening consent present no more than minimal risk to participant. If the participant qualifies to continue with the study after screening, the research assistant conducting the screening will review the Pilot Trial consent with the participant over the phone. When the Little Flower Clinic staff meet with the participant to conduct the Medical Evaluation session they will first review the Pilot Trial consent with the participant and if the participant agrees to continue they will be asked to sign the Pilot Trial consent form at that time. The Pilot Trial consent to be used during COVID-19 restrictions will contain both the name of the staff obtaining informed consent in person and the staff who reviewed the consent over the phone. We have uploaded new consents to use while the COVID-19 restrictions are in place, which a version indicating where changes have been made compared to the previously approved version. Once COVID-19 restrictions are lifted the previously approved process of documented informed consent will resume.
Participants will be encouraged to call the Principal Investigator if any questions arise during the course of the research. Phone numbers for the PI and the ORI are included in the consent form. It is expected that providing the 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 since the PI will not, on most occasions, be the person originally collecting the data.

☐ 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:

Aim 1: The only link between the participant and the research would be the signed consent document (Option 1).

Aim 2: There is no more than minimal risk to participants in the procedures covered in the Screening consent.

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):

Aim 1: We are requesting a waiver of documented informed consent for the qualitative interview script. The research procedures only involve asking participants questions and they are free to skip any questions. Participants are being asked questions about illegal activities and the principle risk of the research is associated with a breach of confidentiality. The interview will not involve collecting any names or other identifiers (Option 1). Participants will be given the option to sign a stamped consent document if they would prefer.

Aim 2: We also request a waiver of documented informed consent only for the Screening consent for study participants who

are unable to be met with in person to sign a consent form. Given the Kentucky governor's recent declaration of a state of emergency, we have advised our data coordinators to take extra precautions when collecting data from participants. Should either jail be placed on lockdown or UK staff deem it unsafe to do face-to- face interviews with eligible participants, we request that those who are unable to complete a face-to-face screening interview be granted a waiver of documented consent, and their screening interview will be completed over the telephone. Research staff will review the Screening consent form in detail with the participant and answer any questions they may have. Verbal consent will be requested. Whenever possible, face-to-face interviews and documented informed consent will be preferred. No interviews will be administered without written or verbal consent.
A waiver of documented informed consent is not being requested for the Pilot Trial consent.

○ **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.

STUDY PERSONNEL **0 unresolved comment(s)**

Do you have study personnel who will be assisting with the research?
After selecting 'Yes' or 'No' you must click the 'Save Study Personnel Information' button.

◉ Yes ○ No

Manage Study Personnel

Identify other study personnel assisting in research project:

- The individual listed as PI in the 'PI Contact Information' section should NOT be added to this section.
- If the research is required for a University of Kentucky academic program, the faculty advisor is also considered study personnel and should be listed below. ***Residents and students who are PI's are encouraged to designate the faculty advisor or at least one other individual as a contact with an editor role (DP).***
- Role: DP = Editor (individual can view, navigate, and edit the application for any review phase (IR, CR/FR, MR) or 'Other Review", and submit Other Reviews on behalf of the PI.)
- Role: SP = Reader (individual can view and navigate through the currently approved application only.)

To add an individual via the below feature:

- Search for personnel;
- Click "select" by the listing for the person you want to add;
- For each person, specify responsibility in the project, whether authorized to obtain informed consent, AND denote who should receive E-IRB notifications (contact status).

NOTE: Study personnel must complete human subject protection (HSP) and Responsible Conduct of Research (RCR) training before implementing any research procedures. For information about training requirements for study personnel, visit UK's HSP FAQ page, the RCR Getting Started page, or contact ORI at 859-257-9428. If you have documentation of current HSP training other than that acquired through UK CITI, you may submit it to ORI (HSPTrainingSupport@uky.edu) for credit.

Study personnel assisting in research project:

Last Name	First Name	Responsibility In Project	Role	AC	Contact	Degree	StatusFlag	(HSP)	(HSP)Date	(RCR)	Removed?	Last Updated	SFI
Anderson	Brittany	Data Collection	SP	Y	N		P	Y	07/14/2021	Y	N	06/28/2019	N
Bush	Heather	Data Analysis/Processing	SP	N	N		P	Y	06/07/2022	Y	N	11/10/2021	N
Calvert	Joseph	Data Analysis/Processing	SP	N	N		P	Y	03/24/2020	Y	N	03/27/2020	N
Dickson	Megan	Data Analysis/Processing	SP	N	N		P	Y	03/23/2022	Y	N	07/14/2021	N
Flores	Katrin	Project Assistance/Support	SP	Y	N		P	Y	05/22/2022	Y	N	02/05/2020	N
Frost	Kathy	Data Collection	SP	Y	N		P	Y	08/29/2022	Y	N	02/13/2018	N
Hardin	Vicky	Project Assistance/Support	SP	N	N		N	Y	03/03/3000		N	07/17/2019	N
Hopper	Vera	Project Assistance/Support	SP	N	N		N	Y	03/03/3000		N	07/17/2019	N
Knudsen	Hannah	Co-Investigator	SP	Y	N		P	Y	08/06/2020	Y	N	02/13/2018	N
Levi	Mary	Data Analysis/Processing	SP	N	N		P	Y	12/16/2020	Y	N	05/03/2022	N
Lofwall	Michelle	Co-Investigator	SP	Y	N		P	Y	08/04/2020	Y	N	02/13/2018	N
Oser	Carrie	Co-Investigator	SP	Y	N		P	Y	12/08/2021	Y	N	02/13/2018	N
Pike	Erika	Data Analysis/Processing	DP	Y	Y		P	Y	02/16/2021	Y	N	07/17/2019	N
Reynolds	Jennifer	Project Assistance/Support	SP	N	N		N	Y	03/03/3000		N	10/17/2019	N
Seaver	Robert	Data Analysis/Processing	SP	N	N		P	Y	02/16/2021	Y	N	02/13/2018	N
Shalash	Sophia	Project Assistance/Support	SP	N	N		P	Y	03/25/2020	Y	N	03/27/2020	N
Tillson	Martha	Data Analysis/Processing	SP	N	N		P	Y	05/03/2021	Y	N	07/14/2021	N
Walsh	Sharon	Co-Investigator	SP	Y	N		P	Y	01/18/2022	Y	N	02/13/2018	N
Webster	John	Data Analysis/Processing	SP	N	N		P	Y	11/24/2020	Y	N	08/19/2021	N
Winston	Erin	Study Coordinator	DP	Y	N		P	Y	04/12/2021	Y	N	01/06/2020	N
Acree	Tianna	Data Analysis/Processing	SP	N	N		P	Y	11/17/2020	Y	Y	04/11/2022	N
Bailey	Egan	Data Collection	SP	N	N		P	Y	06/14/2021	Y	Y	04/11/2022	N

Last Name	First Name	Responsibility In Project	Role	AC	Contact	Degree	StatusFlag	(HSP)	(HSP)Date	(RCR)	Removed?	Last Updated	SFI
Engle	Sarah	Data Collection	SP	Y	N		P	Y	01/09/2020	Y	Y	04/11/2022	N
Fugate	Layla	Project Assistance/Support	SP	Y	N		N	Y	03/03/3000		Y	04/11/2022	N
Litton	Elyse	Project Assistance/Support	SP	Y	N		P	N	01/29/2019		Y	12/14/2020	N
McIntosh	Amy	Project Assistance/Support	SP	Y	N		N	Y	03/03/3000		Y	04/11/2022	N
Mitchell	Kathleen	Project Assistance/Support	SP	Y	N		N	Y	03/03/3000		Y	10/13/2022	N
Mullins	Jenny	Project Assistance/Support	SP	Y	N		N	Y	03/03/3000		Y	10/13/2022	N
Napier	Ellen	Project Assistance/Support	SP	N	N		N	Y	03/03/3000		Y	10/13/2022	N
Sizemore	Calvin	Project Assistance/Support	SP	Y	N		N	Y	03/03/3000		Y	04/11/2022	N
Sparkman	Deloris	Project Assistance/Support	SP	Y	N		N	Y	03/03/3000		Y	04/11/2022	N
Spicer	Amber	Project Assistance/Support	SP	Y	N		N	Y	03/03/3000		Y	10/13/2022	N
Stamper	Roscoe	Data Collection	SP	N	N		P	N	10/03/2018		Y	12/14/2020	N
Wells	Shelly	Data Collection	SP	N	N		N	Y	03/03/3000		Y	12/14/2020	N
White	Joshua	Project Assistance/Support	SP	N	N		N	Y	03/03/3000		Y	04/11/2022	N
White	Tiffany	Project Assistance/Support	SP	Y	N		N	Y	03/03/3000		Y	04/11/2022	N
Williams	Allyson	Project Assistance/Support	SP	Y	N		N	Y	03/03/3000		Y	04/11/2022	N
Williams	Summer	Project Assistance/Support	SP	Y	N		S	N	02/12/2019	Y	Y	04/11/2022	N

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.

****!!!PLEASE READ!!!** Known Issue: The below text boxes do not allow symbols, web addresses, or special characters (characters on a standard keyboard should be ok). If something is entered that the text boxes don't allow, user will lose unsaved information.**

Workaround(s):

- **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 the 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).

The overall aim of this R34 grant is to examine the feasibility, acceptability, and short-term outcomes associated with an innovative service delivery model to increase adherence to extended-release naltrexone (XR-NTX) during the transition from jail to the community for rural individuals with opioid use disorder (OUD). This study responds to a NIH high-priority area to increase access to evidence-based treatment due to the increasing rates of OUD and related high-risk injection drug practices among individuals in rural Appalachia (Staton-Tindall et al., 2015). The Appalachian region is characterized by the highest rates of morbidity, disability, and impaired quality of life in the nation, attributed in large part to increasing rates of prescription opioid use disorder. Kentucky ranks 3rd in the country for drug-related deaths (AHR, 2016), and the state ranks among the highest in the country for drug-related disease transmission (particularly Hepatitis C [HCV]). Kentucky had the highest rate of new HCV infections in the nation between 2008-2015 (KY Dept. for Public Health, 2017), with rates nearly seven times the national average (Zibbell, 2015). The majority of HCV cases has been linked to prescription opioid injection and needle sharing -- high-risk behaviors that also significantly increase the vulnerability of drug users in this region for new HIV infections.
Research indicates that women drug users are more likely to have injecting intimate partners, engage in sex exchange to obtain drugs, and have a faster trajectory from use to dependence than men (Hernandez-Avila et al., 2004; Fraizyngier et al., 2007; Greenfeld et al., 2010; Prithwish et al., 2007). These issues are even more pronounced in rural Appalachia where poverty and limitations in health care access have been exacerbated by the opioid epidemic. Rural women drug users recruited from jails (not providing XR-NXT) in a recent behavioral intervention trial were shown to have extensive opioid injection histories and high rates of HCV, with most women meeting criteria for opioid use disorder (Staton et al., in press). Coupling the severity of substance use with the fact that rural, Appalachian women suffer from some of the most significant health disparities in the country (American College of Obstetricians and Gynecologists, 2014), research is urgently needed to advance access to OUD treatment with this high-risk, vulnerable, and underserved population. Thus, while men will be included in this trial, women will be oversampled and prioritized for treatment entry.
Extended-release naltrexone (XR-NTX) is an effective, life-saving treatment for OUD (e.g., Syed & Keating, 2013), but it is largely underutilized in the criminal justice system despite significant need. A limited number of randomized clinical trials (RCTs) have shown that pre-release XR-NTX has been associated with reductions in community opioid use relapse compared to standard care (Gordon et al., 2017; Lee et al., 2015). These RCTs have primarily included men, have been situated in prisons, and have focused on re-entry to urban communities (Chandler et al., 2016). Research is limited on service delivery models to increase post-release acceptance and adherence to XR-NTX, which is critically needed in rural areas where services are limited. This application proposes to leverage real-world, accessible locations as service delivery models to increase access to evidence-based XR-NTX treatment.

Objectives

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

Specific Aim 1: Adapt the standard XR-NTX protocol for use in a community P&P office for rural individuals with OUD. Adaptation of standardized clinical procedures (ASAM, 2015) will include screening, medical evaluation, injection administration/dosing, safety procedures, and client education materials for delivery in a real-world, non-clinical setting. This aim will be guided by the evidence-based ADAPT-ITT framework and involve key stakeholders (n=10) and rural individuals with OUD(n=20). A second set of qualitative interviews will be conducted with key stakeholders (n=15) and rural individuals with who have used opioids and are incarcerated or on community supervision (n=15) to better understand study trends related to medications for opioid use disorder (MOUD), as well as factors which may affect the feasibility and acceptability of a larger trial (the overall goal of this R34 pilot trial).
Specific Aim 2: Conduct a small scale pilot to examine feasibility, acceptability, and short-term outcomes of the adapted protocol on

XR-NTX adherence and relapse to opioid use. Rural justice-involved individuals on community supervision with OUD will be invited to initiate XR-NTX and continue injections for up to three months in the community.

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.

During this 36-month R34 developmental trial, we propose to examine the feasibility, acceptability, and short-term outcomes associated with an innovative XR-NTX re-entry delivery model to increase adherence during the transition from jail to the community for rural individuals with opioid use disorder (OUD). The study will be accomplished through two specific aims: (1) Adapt XR-NTX services for rural individuals with OUD in the community supervision (P&P) office. This aim focuses on adapting standard clinical procedures (ASAM, 2015) including screening, assessment, injection administration/dosing, safety procedures, and client education materials for a real-world, non-clinical setting (community P&P office) using the evidence-based ADAPT-ITT framework. (2) Conduct a small scale pilot to examine feasibility, acceptability, and short-term outcomes of the adapted protocol on XR-NTX adherence and relapse to opioid use. Rural justice-involved individuals on community supervision with OUD will be invited to initiate XR-NTX and continue injections for up to three months in the community at the Little Flower Clinic in Hazard, KY.

Attachments

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

Recruitment for Aim 1 (focus groups) will include phone calls to health and behavioral health care providers and to community supervision officers in District 11 (see recruitment script). Stakeholder who agree to participate in the focus groups (n=10) will be invited to the one-time group which will be scheduled at a convenient community location (Center for Excellence in Rural Health in Hazard, KY). Focus groups will be audio recorded unless anyone objects. The second set of qualitative interviews (n=15) will be recruited in the same manner, individuals who agree to participate will be invited to complete a group or one-on-one interview which will be scheduled at a convenient community location, over secure video conferencing (i.e., Zoom), or over the phone. Interviews will be audio recorded unless anyone objects.
Recruitment for Aim 1 (focus groups) with incarcerated participants (n=20) will mirror the pilot trial. Consistent with approaches used in our current R01 trial (Staton-Tindall et al., 2015b), participant recruitment in the jail will occur once a month based on a randomized schedule involving days of the week and times of the day. On each monthly recruitment day, a targeted number of offenders serving time in the jail will be randomly sampled from the daily census sheet. All individuals residing in the jail on the day of screening will have an equal opportunity of being selected, including minorities, as long as they are at least 18 years of age and not previously screened for the study. Based on our previous work, and the demography of the overall jail population in rural Appalachia, it is expected that participants will be about 32 years old on average, and 95% will be white (Staton et al., 2017). Focus groups will be audio recorded unless anyone objects. The second set of interviews (n=15) will be recruited by offering the opportunity to complete the interview to those who refuse to participate in the main Vivitrol pilot trial, distributing flyers to those who are on community supervision through the P&P office, distributing flyers at Kentucky River Regional Jail, and distributing flyers in the community (PR stamped and clean flyer attached in the "Advertising" section below). Individuals who agree to participate will be invited to complete a

group or one-on-one interview which will be scheduled at a convenient community location, over secure video conferencing (i.e., Zoom), or over the phone. Interviews will be audio recorded unless anyone objects.
Aim 2: Randomly selected participants will be initially screened to assess recent high-risk opioid use. Face-to-face screening (estimated 10 minutes) will be conducted by the research coordinator. The session will include informed consent and an emphasis on the voluntary nature of participation. Consenting participants will be administered the NIDA-modified ASSIST (NIDA, 2009) to measure high risk opioid use, including injection, prior to entering jail. The ASSIST was developed by the World Health Organization (WHO, 2002) for use in primary health care settings, and modified by NIDA (2009) to separate categories of prescription opioid and street opioid use. Participants in the pilot trial will also be asked about their interest and willingness to engage in XR-NTX treatment, as well as their probation/parole status following release. See additional screening details in "research procedures" below.

**During COVID-19 restrictions, individuals on community supervision who are at high risk for relapse or overdose (as determined by the SSC and/or P&P officer) will be referred to the study for eligibility screening. Once COVID-19 restrictions are lifted, study recruitment will return to previously approved methods. Letters, which briefly explain the study and provide contact information for the study team, will be prepared for mailing by UK staff and provided to P&P (letter is attached in "research procedures" below). P&P will distribute sealed letters to individuals on supervision in Perry County. Flyers (attached in the "Advertising" section) will be distributed to the Perry Co P&P office, KRRJ, and our research office to recruit individuals who may be eligible for Aim 2.
Flyers will be used to recruit individuals to complete interviews for Aim 1 (Flyer interview 2021).
Flyers will be hung at the Perry Co P&P office, at KRRJ, and in our research office to recruit individuals for Aim 2 (Flyer in jail 2021 and Flyer 2021).

Attachments

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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.

All research procedures for Phase 1 (focus groups for intervention development) and Phase 2 (small RCT) including screening, medical evaluation, HIV/HCV testing, baseline interviews, primary measures, and follow-up interviews are discussed in the attached Research Strategy. Also, attached is a medication guide for Vivitrol that will be given to participants. Research procedures to understand study trends related to medications for opioid use disorder (MOUD), as well as factors which may affect the feasibility and acceptability of a larger trial are attached in the Qualitative Interview file.

Follow-up interviews will be conducted in person or over the phone. When UK staff conduct a phone interview they will be in a private location and will encourage the participant to do the same to protect confidentiality.

**During COVID-19 restrictions, we propose several temporary changes to the research procedures, which are outlined in the attached table. Face-to-face procedures will be conducted unless UK research staff are unable to physically meet with the participant due to reasons beyond UK research staff control (e.g., COVID-19 restrictions). Procedures that cannot be shifted to virtual procedures will be conducted by Little Flower Clinic staff during one of the medical sessions. As soon as the jail opens to in person visitors, we will resume normal IRB-approved protocol procedures. A COVID screener (attached) will be used to assess participants for COVID symptoms prior to in person sessions.

Attachments

Attach Type	File Name
ResearchProcedures	2.1b Form_Brief Initial Screening_changes marked.pdf
ResearchProcedures	2.1d Form_Screening Assessment_changes marked.pdf
ResearchProcedures	Vivitrol Protocol Revisions Summary Table 10 1 21 Changes Marked.pdf
ResearchProcedures	XR-NTX Qualitative Interview_ 6 24 21.docx
ResearchProcedures	Letter to P&P_revised_v2.pdf
ResearchProcedures	Letter to P&P_revised_v2_marked.pdf
ResearchProcedures	COVID Screener.pdf
ResearchProcedures	Research Proc 1 3 20 marked.pdf
ResearchProcedures	Research Proc 1 3 20.pdf
ResearchProcedures	Recruitment and Screening_Full Protocol_6 7 19.pdf
ResearchProcedures	Vivitrol info handout.pdf

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.

Data collection for this study will include qualitative data collected from focus groups (audio recorded unless anyone objects) during Phase 1, and Phase 2 RCT data including screening, medical evaluation, interview at baseline, and in person or over the phone follow-up interview (all described in the attached Research Strategy). A DRAFT data collection instrument is included as an attachment.
Aim 1 qualitative interview questions to understand study trends related to medications for opioid use disorder (MOUD), as well as factors which may affect the feasibility and acceptability of a larger trial are attached under the Research Procedures section as the Qualitative Interview.

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 proposed study will use the approach established by our current R01 (IRB #12-0372) in the Kentucky River Regional Jail. The target jail study site has a daily average census of approximately 165 women, and a yearly census of 370 women. Based on our current trial, 80% are anticipated to meet the substance use criteria for the study during the proposed recruitment period (n=296). Based on our previous work with the population, we anticipate 65% of women who are randomly selected for the study will enroll in the protocol. The jails provides medical services and will be available to respond to referrals for HIV/HCV testing procedures if needed. However, because many of the participants in the study are expected to be re-entering the community, HIV/HCV referrals will also be made to local health departments and community based services as well.
Additional available resources for this project include a Principal Investigator with experience in managing clinical research trials (R21-AA017937; R01-11030397), as well as a research staff who work on the current R01 trial with experience with substance users in jails. Co-Investigator Dr. Lofwall is a board-certified psychiatrist and addiction physician in the University of Kentucky Department of Behavioral Science and the Center on Drug and Alcohol Research. Dr. Lofwall has a rich history of conducting medication-assisted treatment including a pivotal study as P.I. for a 36-site Phase III randomized double-dummy double-blind outpatient clinical trial evaluating the efficacy and safety of subcutaneous buprenorphine weekly and monthly injections among adults with moderate – severe opioid use disorder. Dr. Lofwall will oversee all clinical operations including training for the study nurse. She will lead the development of the adapted medication protocol developed during phase one of the study and monitor medication delivery during the RCT open-label trial in phase 2.
Administration of the XR-NTX injections will be carried out under subcontract with The Little Flower Clinic in Hazard, KY. The clinic is designated by the state of Kentucky as a Rural Health Clinic and is a Federally Qualified Health Center. The clinic is a KY DOC contracted site to administer XR-NTX (Vivitrol®) injections and wrap around services, including behavioral therapy, to those released from prison and seeking to obtain help with their addiction in the Hazard/Perry County area. In addition to a team of Nurse Practitioners who will deliver the XR-NTX injections, the clinic has a full-time therapist on staff (LCSW) and a dually licensed Psychiatric Nurse Practitioner. For this project, the Little Flower Clinic will serve as the service provider for XR-NTX, re-entry behavioral therapy, and on-going XR-NTX injections in the treatment-as-usual condition.

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 procedures to be used by this study will involve conventional social science research and treatment methods that are routine in re-entry XR-NTX studies (Lee et al., 2016; Gordon et al., 2017). The potential risks will be discussed with participants during recruitment, screening, and the informed consent process to assist them in making a voluntary decision as to whether they wish to participate in the study protocol. The primary risks associated with participation in this research are those related to oral naltrexone (12.5 mg) and Vivitrol® administration. Naltrexone is an opioid antagonist with little, if any, opioid agonist activity. VIVITROL® (naltrexone for extended-release injectable suspension) is a microsphere formulation of naltrexone for suspension and is administered by intramuscular injection. It is designed as a once-monthly medication for the treatment of opioid dependence, as well as the prevention of relapse to opioid dependence following opioid detoxification.
Potential side-effects of Vivitrol® and oral naltrexone (12.5 mg) will be fully explained to participants during informed consent and will

include the FDA approved package insert for the medication (http://www.alkermes.com/products/vivitrol). The most common side effects of both oral naltrexone and Vivitrol® include nausea, tiredness, headache, dizziness, vomiting, decreased appetite, painful joints, and muscle cramps. In addition, common side effects may also include cold symptoms, trouble sleeping, and toothache. Possible side effects also include risk of opioid overdose if the participant attempts to use large amounts of opioids after returning to the community or possibly overcome the opioid-blocking effects of the medication. Specifically for Vivitrol®, it is also possible that participants may experience injection site reactions, including intense pain, swelling, lumps, blisters, open wound, or a dark scab. Naltrexone may also be associated with increasing the risk for liver damage or hepatitis. While the medical evaluation for this protocol will include a liver function test, participants will also be monitored closely through the trial for symptoms of liver problems including stomach area pain lasting more than a few days, yellowing of the whites of the eyes, dark urine, and tiredness. Other possible side effects include depressed mood, allergic pneumonia, and serious allergic reactions. The risk of serious adverse effects is low, especially using our screening procedures to exclude those that need inpatient detoxification or with LFTs five times the upper limit of normal. The study protocol that is developed for Aim 1 will also include additional study procedures, medical staff coverage, and other strategies for handling any potential adverse events.
In addition to possible risks associated with the medications, other potential psychological risks are primarily related to being asked questions in the interview that they do not feel comfortable asking. It is possible, that a participant may experience anxiety, emotional distress, or other negative reactions due to the content of the interview questions, HIV/HCV testing procedures, and/or treatment participation. Based on our experiences working with this population, such occurrences are rare. Participants will be assured that they do not need to answer anything they do not feel comfortable answering and that they can withdraw at any time with referrals to the local Little Flower Clinic for any medical concerns. These risks will be discussed with each potential study participant during the informed consent process, as well as safeguards in place to provide study protections. If the participant's anxiety reaches a significant concern for the participant, she/he will be removed from the study and provided with a referral for mental health and substance abuse treatment in the community.
The proposed study has potential benefits. First, study participants will have equal opportunity to be screened for high-risk opioid use and opioid use disorder. Second, participants will have the opportunity to participate in a thorough medical evaluation including urinalysis, pregnancy testing, LFT, and HIV and HCV pre-test counseling and testing with results provided during the baseline. Some previous research in by our team has indicated that volunteers have directly benefited from the screening and medical evaluation in cases where abnormal clinical and/or laboratory findings were detected that resulted in treatment of these problems. Third, based on the empirical support for XR-NTX, it is expected that study participants will benefit from receiving the medication and addiction services to decrease illicit drug use and reduce risk for relapse and overdose during the high-risk period of community re-entry. Fourth, there will be significant potential benefits to science because the study will provide important information about the feasibility, acceptability, and short term outcomes associated with an effective, life-saving medication for opioid dependence among high-risk women in rural areas who otherwise face enormous challenges to accessing treatment. Finally, the project will generate important information related to the feasibility of XR-NTX treatment for rural drug users, providing the formative work needed to advance access to treatment through criminal justice venues which can be tailored to high-risk and underserved populations.

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).

There are no alternatives to participation in this evaluation project except not participating.

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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

Self-reported behavioral data and medical information will be collected at screening, medical evaluation, baseline, and 3 months post-release from jail for follow-up interviews, along with HIV/HCV Orasure tests. The study interviewer will attend an intensive week-long training that covers topics including human subjects protection and issues that could arise during jail-based data collection. For example, training will be conducted on the importance of ensuring that all materials brought in to the jail are also taken out of the jail by the interviewers (e.g., pens, study materials, etc). A variety of behavioral data including demographic characteristics, past drug use, injection drug use, health and mental health problems, and service utilization will be collected through self-reports using Computer Assisted Personal Interviewing. administration with a portable computer (DELL notebook). During the CAPI portion of the interview, the trained interviewer will read the instructions, questions, and response categories from a laptop and directly enter the participant's response. The CAPI formatting will be programmed using Questionnaire Development System (QDS™) from Nova Research (http://www.novaresearch.com). Data with the participant ID and all other identifying information (consent form, locator sheet, payment forms) will be stored separately. Consent forms, locator sheets, and payment forms will be managed on site. Security of the data will be maintained through regular computer server backups and CD Rom back-ups secured in fire-safe locked boxes. No data will be provided to jail officials or any other criminal justice official.

Every effort will be made in the protection of human participants and issues relating to participant confidentiality. Because this study will involve individuals who are incarcerated, this study's human participants' protocol will comply fully with the special protections pertaining to behavioral research involving prisoners as participants. A Certificate of Confidentiality will be obtained from the National Institute on Drug Abuse which, under federal statute PL 94 255, prohibits all data collected during the course of a study protocol from being used in any legal or criminal proceedings. Participants will receive a copy of the Certificate of Confidentiality. In addition, participants will be verbally informed and given a copy of the signed informed consent, which describes the study purpose and the confidentiality safeguards. As such, no self-reported data will be shared with anyone outside of approved key personnel. No criminal justice authorities will have access to the self-reported data collected in the interviews or to the clinical data collected during individual sessions. All research data will be kept in locked file cabinets in the office of the Principal Investigator at the University Of Kentucky Department of Behavioral Science. Each participant will receive a unique identifying number. All research data collection instruments will be identified by this number only. The master list matching identifiers to specific participants will be maintained in a locked file in the PI's office. Research data will be reported in aggregate form only. Computer files will be retained and all electronic data will be password protected, stored on secure UK-maintained servers, and accessible only be the researchers on this study. In addition, no DOC personnel (including jail staff or personnel, probation/parole officers, etc) will be asked about participants information for locating and tracking for follow-up. The consent form includes a statement about access to state-maintained records including the KOMS system (Kentucky Offender Management System) which is standard for offender protocols at UK CDAR. Information on participants in the study should be available from those systems and through self-reported locator information. While every effort will be made to keep study information confidential, one arm of the study will be receiving on-going injections in the P&P office. Participants will reminded that no study information will be shared with their officers, but it may be possible for the officer to see them visiting with the study nurse.

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) will stored in the password protected medical database that has limited to only the study nurse, Dr. Lofwall, and Dr. Staton. Incidental materials containing subject identifiers will be shredded. Identification and access of identified data/specimens will be available only to study investigators when it is detrimental to subject safety or the conduct of the research protocol.

Medical risks to study participants will be minimized by thorough medical evaluations, standardized injection procedures, ongoing regular check-in calls with the study nurse, and 24-hour 7 day per week medical on-call medical. Precipitated withdrawal is minimized due to the induction procedure that includes initiation of Vivitrol® dosing during incarceration following opioid detox. The use of the 12.5 mg oral naltrexone challenge and 2 hour wait period will ensure there is no precipitated withdrawal (as evidence by use of COWS) prior to the injection, as well as ensuring that the injection is only given to those participants without any opioid physical dependence. Ensuring no precipitated withdrawal with oral naltrexone prior to the injection is accepted (Gordon et al., 2015; Lee et al., 2017), and Dr. Lofwall's has clinical experience inducting patients in this manner. Thus, it is unlikely that there will be precipitated withdrawal during XR-NTX induction among subjects using full agonist opioids in this study. Additionally, LFTs are evaluated as part of the medical evaluation. The proposed dosing of Vivitrol® is within the therapeutic dose range indicated by the FDA-approved drug label. Vivitrol® will be stored and dispensed through the Little Flower Clinic by licensed nurse practitioners in accordance with federal and state laws. For on-going dosing in the community, if a participant presents to either community site (The Little Flower Clinic or the P&P office) for injections and appears intoxicated, the study nurse will assess the person based on the safety protocol established during Aim 1, and consistent with the protocol for The Little Flower Clinic. In most cases, the injection will be held and a safe ride home will be arranged with a next day (if after 5pm) or same-day medical evaluation (if prior to 5pm) at the Little Flower Clinic to determine the need for any further course of action. Treatment response will be monitored on a regular basis by the study nurse, and counseling and medical staff at the Little Flower Clinic will work closely with participants to help them address ongoing illicit drug use and relapse, which are inherent aspects of opioid dependence.

Participants will also work closely with staff at the Little Flower Clinic to obtain birth control during the course of the study due to the potential consequences of unintended pregnancy among women maintaining XR-NTX (Heil et al., 2016). Any participant becomes pregnant during the study will be removed from the study and referred to substance abuse program that regularly treats pregnant women with OUD. Alternatively, if the woman desires detoxification, she will be referred to the detox program within 24 hours at the Appalachian Regional Hospital in Hazard. All participants, regardless of completing or not completing the study, are offered assistance with finding ongoing treatment in the community (such as The Little Flower Clinic) in order to further decrease the risk of relapse and ongoing illicit drug use.

A Certificate of Confidentiality has been obtained from the National Institute on Drug Abuse which, under federal statute PL 94-255, prohibits all data collected during the course of a study protocol from being used in any legal or criminal proceedings. In addition, participants will be verbally informed and given a copy of the signed informed consent, which describes the study purpose and the

confidentiality safeguards including the Certificate of Confidentiality. As such, no self-reported data will be shared with anyone outside of approved key personnel. No criminal justice authorities will have access to the self-reported data collected in the interviews or to the intervention data collected through the closed, on-line sites.

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

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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.

Aim 1: Participants will receive $25 or a UK promotional item for completing the interview.

Aim 2: Participants will receive $25 for taking part in the screening, $25 research interviews for study at baseline and at follow-up (3-months post release). And, if participants complete all data collection activities, they can earn an additional $25. Participants will have the opportunity to earn up to $100 over the 3 months.

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 is no cost to participants in the 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.

The study Data Safety and Monitoring Plan is included as an attachment.

Future Use and Sharing of Research Data

If the results of 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

Data will not be used for other studies or shared.

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.

HIV/HCV testing procedures are covered under Research Procedures. Testing procedures will be using FDA and CDC approved for ORAQUICK Advance® HIV and HCV Rapid Testing. Testing of subjects will be conducted on a voluntary basis at all interview contacts. As such, none of the subjects will be coerced in any way to submit to testing. They will also be asked to consent for release of any positive HIV screen to the state Department for Public Health in Frankfort knowing that a HIV care coordinator may be contacting them for additional follow-up. In addition: (a) HIV/HCV test results collected at the initial assessment points will be used for research purposes only and will not be made available to correctional or treatment program authorities; (b) all HIV/HCV testing will include pre- and post-test counseling following Centers for Disease Control and Prevention (CDC) protocols; (c) subjects testing positive for HIV/HCV infection will be given referral information as to the appropriate community resources for counseling and treatment, and assisted in contacting these agencies if they so desire it.

PI-Sponsored FDA-Regulated Research

Is this an investigator-initiated study that:

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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).

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

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:

Oral naltrexone tablet
Depot IM naltrexone (Vivitrol)

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:

UK Center on Drug and Alcohol Research
Little Flower Clinic (Hazard, KY)

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

○ Yes ◉ No

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

IND Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

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 Attachment_final.pdf
Study Drug Form	FDA approved label_oral naltrexone.pdf
Study Drug Form	FDA approved label_depot naltrexone.pdf

STUDY DEVICE INFORMATION

0 unresolved comment(s)

A DEVICE may be a:

- component, part, accessory;
- assay, reagent, or in-vitro diagnostic device;
- software, digital health, or mobile medical app;
- other instrument if intended to affect the structure or function of the body, diagnose, cure, mitigate, treat or prevent disease; or
- a homemade device developed by an investigator or other non-commercial entity and not approved for marketing by FDA.

For additional information, helpful resources, and definitions, see ORI's Use of Any Device Being Tested in Research web page.

Does this protocol involve testing (collecting safety or efficacy data) of a medical device including an FDA approved device, unapproved use of an approved device, humanitarian use device, and/or an investigational device?

○ Yes ◉ No

[Note: If a marketed device(s) is only being used to elicit or measure a physiologic response or clinical outcome, AND, NO data will be collected on or about the device itself, you may answer “no” above, save and exit this section, (Examples: a chemo drug study uses an MRI to measure tumor growth but does NOT assess how effective the MRI is at making the measurement; an exercise study uses a heart monitor to measure athletic performance but no safety or efficacy information will be collected about the device itself, nor will the data collected be used for comparative purposes against any other similar device).]

If you answered yes above, please complete the following questions.

LIST EACH DEVICE BEING TESTED IN STUDY IN THE SPACE BELOW

Device Name:

Is the study being conducted under a valid Investigational Device Exemption (IDE), Humanitarian Device Exemption (HDE) or Compassionate Use?

○ Yes ○ No

If Yes, complete the following:
IDE or HDE #(s)

IDE/HDE Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

Other: ☐ Held By:

☐ Check if this is a Treatment IDE or Compassionate Use under the Food and Drug Administration (FDA) Expanded Access program.

For Individual or Small Group Expanded Access, see FDA's Early Expanded Access Program Information, and attach the following:

- FDA expanded access approval or sponsor’s authorization;
- An independent assessment from an uninvolved physician, if available;
- 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 Medical Device SOP.

Does the intended use of any research device being tested (not clinically observed) in this study meet the regulatory definition of Significant Risk (SR) device?

- Yes. Device(s) as used in this study presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
- No. All devices, as used in this study do not present a potential for serious risk to the health, safety, or welfare of subjects/participants.

Complete and attach the required Study Device Form, picking the "Study Device Form" for the document type. Any applicable device documentation (e.g., Manufacturer information; patient information packet; approved labeling; FDA correspondence, etc.) should be attached using "Other Device Documentation" for the document type.

Attachments

RESEARCH SITES

0 unresolved comment(s)

To complete this section, ensure the responses are accurate then click "SAVE".

A) Check all the applicable sites listed below at which the research will be conducted. If none apply, you do not need to check any boxes.

UK Sites

- ☐ UK Classroom(s)/Lab(s)
- ☐ UK Clinics in Lexington
- ☐ UK Clinics outside of Lexington
- ☐ UK Healthcare Good Samaritan Hospital
- ☐ UK Hospital

Schools/Education Institutions

- ☐ Fayette Co. School Systems *
- ☐ Other State/Regional School Systems
- ☐ Institutions of Higher Education (other than UK)

***Fayette Co. School systems, as well as other non-UK sites, have additional requirements that must be addressed. See ORI's IRB Application Instructions - Off-site Research web page for details.**

Other Medical Facilities

- ☐ Bluegrass Regional Mental Health Retardation Board
- ☐ Cardinal Hill Hospital
- ☐ Eastern State Hospital
- ☐ Norton Healthcare
- ☐ Nursing Homes
- ☐ Shriner's Children's Hospital
- ☐ Veterans Affairs Medical Center
- ☐ Other Hospitals and Med. Centers

- ☑ Correctional Facilities
- ☐ Home Health Agencies
- ☐ International Sites

Research activities conducted at performance sites that are not owned or operated by the University of Kentucky, at sites that are geographically separate from UK, or at sites that do not fall under the UK IRB's authority, are subject to special procedures for coordination of research review. Additional information is required (see IRB Application Instructions - Off-Site Research web page), including:

- A letter of support and local context is required from non-UK sites. See *Letters of Support and Local Context* on the IRB Application Instructions - Off-Site Research web page for more information.
- Supportive documentation, including letters of support, can be attached below.
- NOTE: If the non-UK sites or non-UK personnel are engaged in the research, there are additional federal and university requirements which need to be completed for their participation. For instance, the other site(s) may need to complete their own IRB review, or a cooperative review arrangement may need to be established with non-UK

sites.
- Questions about the participation of non-UK sites/personnel should be discussed with the ORI staff at (859) 257-9428.

List all other non-UK owned/operated locations where the research will be conducted:

Kentucky River Regional Jail
The Little Flower Clinic-an FWA for Little Flower has been obtained due to NIH funding requirements, and the IAA to reflect that agreement is attached to the application.

Describe the role of any non-UK site(s) or non-UK personnel who will be participating in your research.

Attachments

Attach Type	File Name
-IRB Approval (non-UK)	Fully executed IAA for Staton 43830 between UK and Little Flower Clinic.pdf
-Letter of Support & Local Context	PerryCoLOS.pdf
-Letter of Support & Local Context	LittleFlowerClinic_letter.pdf

B) Is this a multi-site study for which **you are the lead investigator or UK is the lead site**? ○ Yes ◉ No

If YES, describe the plan for the management of reporting unanticipated problems, noncompliance, and submission of protocol modifications and interim results from the non-UK sites:

C) If your research involves collaboration with any sites and/or personnel outside the University of Kentucky, then it is considered multisite research and IRB reliance issues will need to be addressed. This may include national multi-center trials as well local studies involving sites/personnel external to UK. If you would like to request that the University of Kentucky IRB (UK IRB) serve as the lead IRB for your study, or if you would like the UK IRB to defer review to another IRB, please contact the IRBReliance@uky.edu.

RESEARCH ATTRIBUTES

0 unresolved comment(s)

Indicate the items below that apply to your research. Depending on the items applicable to your research, you may be required to complete additional forms or meet additional requirements. Contact the ORI (859-257-9428) if you have questions about additional requirements.

☐ Not applicable

Check All That Apply

	For additional requirements and information:
☐ Academic Degree/Required Research	• Cancer Research (MCC PRMC) • Certificate of Confidentiality (look up "Confidentiality/Privacy...") • CCTS (Center for Clinical and Translational Science)
☑ Alcohol/Drug/Substance Abuse Research	• Clinical Research (look up "What is the definition of....)
☐ Biological Specimen Bank Creation (for sharing)	• Clinical Trial
☐ Cancer Research	• Collection of Biological Specimens for Banking (look up "Specimen/Tissue Collection...")
☐ CCTS-Center for Clinical & Translational Science	• Collection of Biological Specimens (look up "Specimen/Tissue Collection...")
☑ Certificate of Confidentiality	• Community-Based Participatory Research (look up "Community-Engaged...")
☐ Clinical Research	• Data & Safety Monitoring Board (DSMB) *For Medical IRB: Service Request Form for CCTS DSMB
☐ Clinical Trial - Phase 1	
☑ Clinical Trial	
☐ Collection of Biological Specimens for internal banking and use (not sharing)	• Data & Safety Monitoring Plan
☐ Community-Based Participatory Research	
☐ Deception	• Deception* *For deception research, also go to the E-IRB Application Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"
☐ Educational/Student Records (e.g., GPA, test scores)	
☐ Emergency Use (Single Patient)	• Emergency Use (Single Patient) [attach Emergency Use Checklist] (PDF)
☐ Gene Transfer	• Genetic Research (look up "Specimen/Tissue Collection...")
☐ Genetic Research	• Gene Transfer
☐ GWAS (Genome-Wide Association Study) or NIH Genomic Data Sharing (GDS)	• HIV/AIDS Research (look up "Reportable Diseases/Conditions")
☐ Human Cells, Tissues, and Cellular and Tissue Based Products	• Screening for Reportable Diseases [E2.0000] (PDF)
☐ Individual Expanded Access or Compassionate Use	• International Research (look up "International & Non-English Speaking")
☐ International Research	• NIH Genomic Data Sharing (GDS) Policy (PDF)
☐ Planned Emergency Research Involving Exception from Informed Consent	• Planned Emergency Research Involving Waiver of Informed Consent* *For Planned Emergency Research Involving Waiver of Informed Consent, also go to the E-IRB Application Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"
☐ Recombinant DNA	
☐ Registry or data repository creation	
☐ Stem Cell Research	
☐ Suicide Ideation or Behavior Research	• Use, storage and disposal of radioactive material and radiation producing devices
☐ Survey Research	
☐ Transplants	
☐ Use, storage and disposal of radioactive material and radiation producing devices	
☐ Vaccine Trials	

FUNDING/SUPPORT

0 unresolved comment(s)

If the research is being submitted to, supported by, or conducted in cooperation with an external or internal agency or funding program, indicate below all the categories that apply.

☐ Not applicable

Check All That Apply

- ☑ Grant application pending
- ☑ (HHS) Dept. of Health & Human Services
  - ☑ (NIH) National Institutes of Health
  - ☐ (CDC) Centers for Disease Control & Prevention
  - ☐ (HRSA) Health Resources and Services Administration
  - ☐ (SAMHSA) Substance Abuse and Mental Health Services Administration
- ☐ (DoJ) Department of Justice or Bureau of Prisons
- ☐ (DoE) Department of Energy
- ☐ (EPA) Environmental Protection Agency
- ☐ Federal Agencies Other Than Those Listed Here
- ☐ Industry (Other than Pharmaceutical Companies)
- ☐ Internal Grant Program w/ proposal
- ☐ Internal Grant Program w/o proposal
- ☐ National Science Foundation
- ☐ Other Institutions of Higher Education
- ☐ Pharmaceutical Company
- ☐ Private Foundation/Association
- ☐ U.S. Department of Education
- ☐ State

Other:

Click applicable listing(s) for additional requirements and information:

- (HHS) Dept. of Health & Human Services
- (NIH) National Institutes of Health
- (CDC) Centers for Disease Control & Prevention
- (HRSA) Health Resources & Services Administration
- (SAMHSA) Substance Abuse & Mental Health Services Administration
- Industry (Other than Pharmaceutical Companies) [IRB Fee Info]
- National Science Foundation
- (DoEd) U.S. Department of Education
- (DoJ) Department of Justice or Bureau of Prisons
- (DoE) Department of Energy Summary and Department of Energy Identifiable Information Compliance Checklist
- (EPA) Environmental Protection Agency

Specify the funding source and/or cooperating organization(s) (e.g., National Cancer Institute, Ford Foundation, Eli Lilly & Company, South Western Oncology Group, Bureau of Prisons, etc.):

National Institute on Drug Abuse

Add Related Grants

If applicable, please search for and select the OSPA Account number or Electronic Internal Approval Form (eIAF) # (notif #) associated with this IRB application using the "Add Related Grants" button.
If required by your funding agency, upload your grant using the "Grant/Contract Attachments" button.

Add Related Grants

Grant/Contract Attachments

Attach Type	File Name
GrantContract	Staton_Christa_3200002279_PADR1.pdf

The research involves use of Department of Defense (DoD) funding, military personnel, DoD facilities, or other DoD resources. (See DoD SOP and DoD Summary for details)

○ Yes ◉ No

Using the “attachments” button (below), attach applicable materials addressing the specific processes described in the DoD SOP.

DOD SOP Attachments

Additional Certification: (If your project is federally funded, your funding agency may request an Assurance/ Certification/Declaration of Exemption form.) Check the following if needed:

☐ Protection of Human Subjects Assurance/Certification/Declaration of Exemption (Formerly Optional Form – 310)

Assurance/Certification Attachments

OTHER REVIEW COMMITTEES

0 unresolved comment(s)

If you check any of the below committees, additional materials may be required with your application submission.

Does your research fall under the purview of any of the other review committees listed below? [*If yes, check all that apply and attach applicable materials using the attachment button at the bottom of your screen.*]

○ Yes ◉ No

Additional Information

- ☐ Institutional Biosafety Committee
- ☐ Radiation Safety Committee
- ☐ Radioactive Drug Research Committee
- ☐ Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)
- ☐ Graduate Medical Education Committee (GME)
- ☐ Office of Medical Education (OME)

- Institutional Biosafety Committee (IBC) - Attach required IBC materials
- Radiation Safety Committee (RSC) - For applicability, see instructions and attach form
- Radioactive Drug Research Committee (RDRC)
- Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)** - Attach MCC PRMC materials, if any, per instructions.
- Office of Medical Education (OME)
- Graduate Medical Education Committee (GME)

Attachments

**** If your study involves cancer research, be sure to select "Cancer Research" in the "Research Attributes" section.** ORI will send your research protocol to the Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC). The MCC PRMC is responsible for determining whether the study meets the National Cancer Institute (NCI) definition of a clinical trial and for issuing documentation to you (the investigator) which confirms either that PRMC approval has been obtained or that PRMC review is not required. Your IRB application will be processed and reviewed independently from the PRMC review.

ADDITIONAL INFORMATION/MATERIALS

0 unresolved comment(s)

Do you want specific information inserted into your approval letter? ◉ Yes ○ No

Approval Letter Details:

If you wish to have specific language included in your approval letter (e.g., serial #, internal tracking identifier, etc…), type that language in the box below exactly as it should appear in the letter. The text you enter will automatically appear at the top of all approval letters, identical to how you typed it, until you update it. Don't include instructions or questions to ORI staff as those will appear in your approval letter. **If these details need to be changed for any reason, you are responsible for updating the content of this field.**

Continuation 2022

Additional Materials:

If you have other materials you would like to include for the IRB's consideration, check all that apply and attach the corresponding documents using the Attachments button below.

- ☑ Detailed protocol
- ☐ Dept. of Health & Human Services (DHHS) approved protocol (such as NIH sponsored Cooperative Group Clinical Trial)
- ☐ Other Documents

Protocol/Other Attachments

Attach Type	File Name
Other	Julia Gorey_101018_114859.pdf
Other	Vivitrol info handout.pdf
Other	FWA.pdf
Other	Fully executed IAA for Staton 43830 between UK and Little Flower Clinic.pdf
Other	Little Flower Clinic Indivdual Invesigator Agreement Forms and Training Documentation.pdf
Protocol	Little Flower Clinic Staff Individual Investigator Forms and Training Documentation.pdf

NOTE: [Instructions for Dept. of Health & Human Services (DHHS)-approved protocol]

If you have password protected documents, that feature should be disabled prior to uploading to ensure access for IRB review.

To view the materials currently attached to your application, click “All Attachments” on the left menu bar.

SIGNATURES (ASSURANCES)

0 unresolved comment(s)

All IRB applications require additional assurances by a Department Chairperson or equivalent (DA), and when applicable, a Faculty Advisor or equivalent (FA). This signifies the acceptance of certain responsibilities and that the science is meritorious and deserving of conduct in humans. The person assigned as DA *should not* also be listed in the Study Personnel section, and the individual assigned as FA *should* be listed in the Study Personnel section.

For a list of responsibilities reflected by signing the Assurance Statement, refer to "What does the Department Chairperson's Assurance Statement on the IRB application mean?"

Required Signatures:

First Name	Last Name	Role	Department	Date Signed	
Carl	Leukefeld	Department Authorization	Behavioral Science	02/15/2018 11:04 AM	View/Sign
Christa	Staton	Principal Investigator	Behavioral Science	02/14/2018 03:27 PM	View/Sign

Department Authorization

☑ This is to certify that I have reviewed this research protocol and that I attest to the scientific validity and importance of this study; to the qualifications of the investigator(s) to conduct the project and their time available for the project; that facilities, equipment, and personnel are adequate to conduct the research; and that continued guidance will be provided as appropriate. When the principal investigator assumes a sponsor function, the investigator has been notified of the additional regulatory requirements of the sponsor and by signing the principal investigator Assurance Statement, confirms he/she can comply with them.

*If the Principal Investigator is also the Chairperson of the department, the Vice Chairperson or equivalent should complete the "Department Authorization".

**IF APPLICABLE FOR RELIANCE: I attest that the principal investigator has been notified of the regulatory requirements of both the Reviewing and Relying IRBs, according to the information provided in the E-IRB application. The attached Reliance Assurance Statement, signed by the principal investigator, confirms that he/she can comply with both sets of IRB requirements.

Principal Investigator's Assurance Statement

I understand the University of Kentucky's policies concerning research involving human subjects and I agree:

1. To comply with all IRB policies, decisions, conditions, and requirements;
2. To accept responsibility for the scientific and ethical conduct of this research study;
3. To obtain prior approval from the Institutional Review Board before amending or altering the research protocol or implementing changes in the approved consent/assent form;
4. To report to the IRB in accord with IRB/IBC policy, any adverse event(s) and/or unanticipated problem(s) involving risks to subjects;
5. To complete, on request by the IRB for Full and Expedited studies, the Continuation/Final Review Forms;
6. To notify the Office of Sponsored Projects Administration (OSPA) and/or the IRB (when applicable) of the development of any financial interest not already disclosed;
7. Each individual listed as study personnel in this application has received the mandatory human research protections education (e.g., CITI);
8. Each individual listed as study personnel in this application possesses the necessary experience for conducting research activities in the role described for this research study.
9. To recognize and accept additional regulatory responsibilities if serving as both a sponsor and investigator for FDA regulated research.

☑ Furthermore, by checking this box, I also attest that:

- I have appropriate facilities and resources for conducting the study;
- I am aware of and take full responsibility for the accuracy of all materials submitted to the IRB for review;
- If applying for an exemption, I also certify that the only involvement of human subjects in this research study will be in the categories specified in the Protocol Type: Exemption Categories section.
- If applying for an Abbreviated Application (AA) to rely on an external IRB, I understand that certain items above (1, 3, 4, 7-8) may not apply, or may be altered due to external institutional/IRB policies. I document my agreement with the Principal Investigator Reliance Assurance Statement by digitally signing this application.

*You will be able to "sign" your assurance after you have sent your application for signatures (use Submission section). Please notify the personnel required for signing your IRB application after sending for signatures. Once all signatures have been recorded, you will need to return to this section to submit your application to ORI.

SUBMISSION INFORMATION

0 unresolved comment(s)

***** If this Continuation Review entails a change in the scope of your activities to include COVID-19 related research, please insert "COVID19" at the start of your Project and Short Titles.*****

Each Section/Subsection in the menu on the left must have a checkmark beside it (except this Submission section) indicating the Section/Subsection has been completed. Otherwise your submission for IRB review and approval cannot be sent to the Office of Research Integrity/IRB.

If applicable, remember to update the Approval Letter Details text box under the Additional Information section

If your materials require review at a convened IRB meeting which you will be asked to attend, it will be scheduled on the next available agenda and you will receive a message to notify you of the date.

If you are making a change to an attachment, you need to delete the attachment, upload a highlighted version that contains the changes (use Document Type of "Highlighted Changes"), and a version that contains the changes without any highlights (use the appropriate Document Type for the item(s)). Do **not** delete approved attachments that are still in use.

Principal Investigator's Assurance Statement

I understand the University of Kentucky's policies concerning research involving human subjects, and I attest to:

1. Having reviewed all the investigational data from this study, including a compilation of all internal and external unanticipated problems.
2. Having reviewed, if applicable, information from the sponsor including updated investigator brochures and data and safety monitoring board reports.

I also attest that I have reviewed pertinent materials concerning the research and concluded either:

A. The human subject risk/benefit relationship is NOT altered, and that it is not necessary to modify the protocol or the informed consent process,
OR,
B. The human subject risk/benefit relationship has been altered, and have previously submitted or am including with this continuation review submission, a modification of the research protocol and informed consent process.

☑ By checking this box, I am providing assurances for the applicable items listed above.

Your protocol has been submitted.

KEY INFORMATION FOR MEDICATIONS FOR RURAL INDIVIDUALS WITH OUD PILOT TRIAL ENROLLMENT
11/9/21

You are being invited to take part in a research study about injectable naltrexone (Vivitrol®) for opioid use disorder (OUD) treatment among rural individuals who transition from jail to the community.

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

There are two purposes for this research. First, we hope to design a medication (injectable naltrexone) protocol to reduce the risk for relapse to opioids among rural individuals during community re-entry. Second, we want to see if individuals who are transitioning from jail to the community or on community supervision will use injectable naltrexone and if it is helpful to them. Your commitment to this research will be participation in the pilot study whereby injectable naltrexone (Vivitrol®), a FDA-approved medication for opioid relapse prevention in people with OUD, is offered to rural individuals with opioid use disorder and on community supervision.

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

There are a few reasons you might volunteer for this study. First, study participants will have equal opportunity to be screened for high-risk opioid use and OUD. Second, participants will have the opportunity to participate in a thorough medical evaluation including urinalysis, pregnancy testing, liver function test. Third, based on the research for injectable naltrexone, it is expected that study participants will benefit from receiving the medication and addiction counseling and case management services to decrease illicit drug use and reduce risk for relapse and opioid-involved overdose. Fourth, there will be significant potential benefits to science because the study will provide important information about the feasibility, acceptability, and short-term outcomes associated with an effective, life-saving medication for opioid use disorder among high-risk individuals in rural areas who otherwise face enormous challenges to accessing treatment. Finally, the project will generate important information related to the feasibility of injectable naltrexone treatment for rural individuals with OUD, providing the needed work needed to advance access to treatment through criminal justice venues which can be tailored to high-risk and underserved populations.

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

You should not participate in this study if you are not currently at least 18 years of age or do not want to use injectable naltrexone in the study. This study is completely voluntary. You should not participate in this study if you are pregnant or intend to become pregnant within the next 3 months. You should also not participate if you are in liver failure, are already in OUD treatment with injectable naltrexone, buprenorphine, or methadone, have chronic pain conditions that require prescription opioids, or untreated medical and/or psychiatric conditions. You should not participate if you do not have or are unwilling to obtain Medicaid or other health insurance. If you choose not to participate in this study, you may choose to find other medical providers to treat you if you have opioid use disorder with injectable naltrexone or another FDA approved medication.

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 benefits or rights you would normally have if you choose not to volunteer. You can stop at any time during the study and still keep the benefits and rights you had before volunteering. If you do not want to take part in this study, it won't affect your status with any criminal justice agency, treatment, parole, or other agency. If you are currently on probation or parole, the researchers will not disclose any information about you or your participation in the study to the parole board or to a parole officer to influence their decisions without your specific written authorization.

WHAT ELSE DO YOU NEED TO KNOW?

If you are under the supervision of the Kentucky Department of Corrections (DOC), (including prisoners, parolees, awaiting sentencing for felony convictions), then note that: The DOC requires researchers to provide the DOC with the name of participants and the title of the research study. By agreeing to be in the study, you are allowing the researcher to provide your name and the study title to the DOC. The information will be sent to the DOC's Director of the Office of Research and Legislative Services in Frankfort. The researcher will not share any of your research data or confidential information with the DOC. The DOC may ask you to sign a separate consent form that verifies that you are volunteering for a study that is not a part of the DOC. If you do not want to sign the DOC consent form, you should not choose to participate in this study, and if you chose not to sign the DOC consent we would have to withdraw you from this study.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of this study is Michele Staton, Ph.D. of the University of Kentucky, Department of Behavioral Science. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study, her contact information is 859-312-8245. 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?

You will not qualify for this study if you meet any of the following criteria: 1) you are currently pregnant, or have a positive pregnancy test during the study medical screening; 2) you do not have a opioid use disorder based on screening; 3) if you are currently in treatment with methadone or buprenorphine; 4) if you have a serious medical or psychiatric condition or abnormal laboratory results that would make it unsafe for you to participate; 5) require opioid analgesics for pain treatment; 6) if you want to hurt yourself or end your life or 7) if you have a body mass index greater than 40. You will also not quality for this study if 8) you are not planning to be released from jail within 3 months and 9) you are not planning to live the Hazard/Perry County area. You will not qualify for the study if 10) you do not have or are unwilling to obtain Medicaid or other health insurance.

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

Because you have participated in the initial screening, you can now be referred for the study medical evaluation with the study nurse from the Little Flower Clinic. The medical evaluation will take place at the Little Flower Clinic in Hazard and it will take approximately 1 hour. If you are medically eligible for the study, you will be asked to complete an interview with a research assistant which will be done in the jail (if you are incarcerated), over the phone, video conference call, or face-to-face at a location that is convenient for you. It will take about 1 - 2 hours and will include questions about your drug use, health, and related issues. You will also be given an injection of injectable naltrexone and you will be asked to continue the injectable naltrexone injections for up to 3 months in the community where you will continue to meet with the study staff from the Little Flower Clinic at the Little Flower Clinic in Hazard. The research assistant will also talk with you one more time in three months. It will be for an interview over the phone, a video conference call, or at a place that is convenient for you, and it will also take about 1-2 hours. The total amount of time you will be asked to volunteer for data collection and medication visit sessions for this study is 10-12 hours over the next 3 months. The following table shows visits and time commitments:

Visit	Description	Time commitment
Initial screening session	Completion of surveys to determine eligibility	2 hours
Initial study data collection interview	Interview with UK research assistant	1-2 hours
Medical evaluation	Medical assessment for study eligibility at the Little Flower Clinic in Hazard	1 hour
First injection	Visit with nurse to get first injectable naltrexone injection, visit with therapist, and visit with case manager at the Little Flower Clinic in Hazard	Up to 3 hours
2nd injection in community after release (30 days after first injection)	Visit with nurse to get injectable naltrexone injection, visit with therapist, and visit with case manager at the Little Flower Clinic in Hazard	Up to 2 hours
3rd injection in community after release (30 days after 2nd injection)	Visit with nurse to get injectable naltrexone injection, visit with therapist, and visit with case manager at the Little Flower Clinic in Hazard	Up to 2 hours
4th injection in community after release (30 days after 3rd injection)	Visit with nurse to get injectable naltrexone injection, visit with therapist, and visit with case manager at the Little Flower Clinic in Hazard	Up to 2 hours
Follow-up study data collection interview in 3 months	Interview with UK research assistant	1-2 hours

WHAT WILL YOU BE ASKED TO DO?

If you screen eligible to participate in the study, you will be asked to participate in a medical evaluation at the Little Flower Clinic in Hazard. As part of the medical evaluation, you will be asked a number of questions pertaining to your medical history. The nurse will also check your vital signs and collect a blood sample to help evaluate your basic body functioning (like your liver and kidney functioning, blood sugar, electrolyte and fluid balance) to help ensure that you are healthy enough to enter the trial. If you do not currently have Medicaid or other health insurance coverage, case managers at the Little Flower Clinic can assist with the process to get you enrolled.

If you meet all of the study eligibility criteria, you will be asked to complete a face-to-face, phone, or video conference call interview with a UK research assistant about your history of substance use, sexual activity, mental health, criminal justice involvement, need for treatment, and feelings/attitudes about treatment. After completion of the

interview, the study nurse will schedule another visit with you at the Little Flower Clinic in Hazard and will ask you to take a 12.5 mg low dose oral naltrexone tablet to confirm that you are not physically dependent on opioids anymore and that you are ready for the injection of injectable naltrexone. The nurse will monitor you for any potential side effects for 2 hours after that oral dose, and if no signs of opioid withdrawal are noted, your first injectable naltrexone dose (380 mg) will be administered via injection into a buttock right under your beltline. You will be given a card with the contact information for the study nurse, as well as our study physician (Dr. Jenny Mullins) and Dr. Staton (study Principal Investigator) if you have any issues with the injectable naltrexone dose.

You will be eligible for a monthly injection at the Little Flower Clinic (421 Memorial Drive, Hazard, KY) every 30 days for 3 months and the study nurse will contact you with a reminder for those injections. You will also meet with a therapist and a case manager from the Little Flower Clinic as part of your treatment. Through this study, you will be given up to 3 injections in the community. Our staff will assist you with resources needed to continue treatment after the end of the study, however, no guarantee of insurance coverage or other needed resources is being made.

Both groups will be asked to provide urine samples for drug testing on the days of the community injections and these samples may be observed by a member of the research team. All samples will be observed by a trained, same-sex staff member, meaning only female staff will observe samples provided by female participants and male staff will observe samples provided by male participants.

Both groups will be asked to take part in the baseline interview and 3-month follow-up interview with a UK research assistant. Questions in the follow-up interview will be very similar to the earlier interview regarding drug use and related issues. However, it will also ask about any personal changes in the services that you receive, as well as to provide a urine sample for a drug screen (if the interview is completed in person). In order to stay in touch with you for follow-up, you will also be asked to give locator information during your initial interview. This includes the names, addresses, and phone numbers of individuals who would be most likely to know how to reach you. You are also asked to let the research team access information in state-maintained records (DOC KOMS files, behavioral health service records) including admission/discharge/termination dates of treatment services, number and kind of services received, discharges, diagnosis/other relevant clinical information, court dates and actions, results of urine screens, time incarcerated, and other criminal activity in the study. The research team may also use other internet searches and social media sites like Facebook to try to find you for the follow-up. Please note that if you are in a residential treatment program or a jail facility at the time of your 3-month follow-up, the research team will attempt to contact you there to do your follow-up.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

The primary risks associated with participation in this research are those related to oral naltrexone tablet (12.5 mg) and injectable naltrexone injection administration. You will be provided with a copy of the FDA medication guide for injectable naltrexone which explains all possible side effects. Naltrexone is an opioid antagonist with little, if any, opioid agonist activity. In other words, you will not get “high” as a result of taking this medication. While the risk of serious adverse effects is low, especially using our screening procedures, we want to make you aware that there are some possible side effects of using naltrexone. The most common side effects of both medications include nausea, tiredness, headache, dizziness, vomiting, decreased appetite, painful joints, and muscle cramps. In addition, common side effects may also include cold symptoms, trouble sleeping, and toothache. Possible side effects also include risk of opioid overdose if you attempt to use large amounts of opioids after returning to the community. Therefore, use of injectable naltrexone may require a different pain management strategy in an emergency situation or if surgery is required. Specifically, for injectable naltrexone, it is also possible that you may experience injection site reactions, including intense pain, swelling, lumps, blisters, open wound, or a dark scab. An injection site reaction could be severe and require medical intervention. Naltrexone may also be associated with increasing the risk for liver damage or hepatitis. While the medical evaluation for this protocol will include a liver function test to rule out any liver complications, you will also be monitored closely through the trial for symptoms of liver problems including stomach area pain lasting more than a few days, yellowing of the whites of the eyes, dark urine, and tiredness. Other possible side effects include depressed mood (which may be associated with suicidal thoughts), allergic pneumonia, and serious allergic reactions.

In addition to possible risks associated with the medications, other potential psychological risks are primarily related to being asked questions in the interview that you do not feel comfortable asking. It is possible, that you might experience anxiety, emotional distress, or other negative reactions due to the content of the interview questions, HIV/HCV testing procedures, and/or treatment participation. Based on our experiences working with this population, such occurrences are rare. Please know that you do not need to answer anything you do not feel comfortable

answering and you can withdraw at any time with referrals to the local Little Flower Clinic for any medical concerns. 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?

There is no guarantee that you will get any benefit from taking part in this study. However, some people have experienced success with injectable naltrexone in reducing the risk for relapse to opioids.

WHAT WILL IT COST YOU TO PARTICIPATE?

There is no cost to you for participating in the study. If there are other costs to you for any health conditions, you and/or your insurance company, Medicare, or Medicaid will be responsible for the costs of all care and treatment that you would normally receive. These are costs that are considered medically necessary and will be part of the care you receive even if you do not take part in this study.

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

We will make every effort to keep private 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 on everyone in the study. You will not be personally identified in these papers or reports. We may publish the results of this study; however, we will keep your name and other identifying information private.

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. All research data will be kept in locked file cabinets in the office of the Principal Investigator at the University of Kentucky Department of Behavioral Science. Your research records with us will not include your name – we assign only a number to your file. All research data will be identified by this number only. Some of your information including demographics, substance use and medical history, screening and lab results, medication monitoring, and clinical notes will be shared between the research team at the University of Kentucky and the Little Flower Clinic in order to provide the best care possible during this medication trial. Any clinical files with the Little Flower Clinic that contain your name will be kept separate from your research data. Computer files will be retained and all electronic data will be password protected, stored on secure UK-maintained servers, and accessible only to the researchers on this study.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate 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. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

Officials from the National Institutes of Health (National Institute on Drug Abuse, which funds this study) and the University of Kentucky may look at or copy pertinent portions of records that identify you. In addition, if you test positive for HIV or HCV and release your test result, that information will also be shared with the Kentucky Department of Public Health. However, it is the policy of these agencies and these investigators that every attempt will be made to resist demands to release information that identifies you. When results of this study are published, your name will not be used.

CAN YOU CHOOSE TO WITHDRAW FROM THE STUDY EARLY?

If you decide to take part in the study you still have the right to decide at any time that you no longer want to continue. You will not be treated differently if you decide to stop taking part in the study. If you decide to stop the injectable naltrexone treatment, we would still like to do a 3-month follow-up interview. The individuals conducting the study may need to withdraw you from the study. This may occur if you have an unexpected reaction to the study medication, if you are not able to follow the directions they give you, if they find that your being in the study is of more risk than benefit to you, or if the agency funding the study decides to stop the study early for a variety of reasons. If you become pregnant during the course of the 3-month study trial, you will not be able to continue on study medication, but you are still invited to continue with the research study visits. the research team will provide you with a referral to treatment specifically for pregnant women. Should you withdraw or be withdrawn, data collected up to that point will be kept.

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

You cannot take part in this study if you are enrolled in any other study involving the delivery of medication for opioid use disorder (such as methadone or buprenorphine) or another investigational medication or device. It is important to let the investigator/your doctor know if you are in another research study. You should also discuss with the investigator before you agree to participate in another research study while you are enrolled 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 due to the study, you should call Michele Staton, PhD, (859-312-8245) or the study physician Jenny Mullins, DO (606-487-9505) immediately. You may also call the study nurse, Allyson Williams, at the Little Flower Clinic at (606-487-9505). Study staff will determine what type of treatment, if any, that 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. Therefore, these costs 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.

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

You will receive $25 for taking part in the research interviews for this study at baseline, $25 at follow-up (3-months post release), and a $25 completion bonus for all data collection activities. With the additional $25 you earned for screening, you will have the opportunity to earn up to $100 over the next 3 months. If you earn $600 or above by participating in research in one year, it is potentially reportable for tax purposes. You will also receive up to 4 injections of injectable naltrexone at no cost to you.

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.

WILL YOU BE GIVEN INDIVIDUAL RESULTS FROM THE RESEARCH TESTS?

Michele Staton, Principal Investigator, will contact you with information about research results or incidental findings that are determined to be important to you/your family's health. (Incidental findings are unforeseen findings discovered during the course of the research that may affect you or your family's health).

WHAT ELSE DO YOU NEED TO KNOW?

If you volunteer to take part in this study, you will be one of about 60 individuals to do so through the University of Kentucky. The National Institute on Drug Abuse is providing financial support and/or material for this study. Alkermes is providing the injectable naltrexone for this study.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

If you are under the supervision of the Kentucky Department of Corrections (DOC), (including prisoners, parolees, awaiting sentencing for felony convictions), then note that: The DOC requires researchers to provide the DOC with the name of participants and the title of the research study. By agreeing to be in the study, you are allowing the researcher to provide your name and the study title to the DOC. The information will be sent to the DOC's Director of the Office of Research and Legislative Services in Frankfort. The researcher will not share any of your research data or confidential information with the DOC. The DOC may ask you to sign a separate consent form that verifies that you are volunteering for a study that is not a part of the DOC. If you do not want to sign the DOC consent form, you should not choose to participate in this study, and if you chose not to sign the DOC consent we would have to withdraw you from this study.

FUTURE USE OF YOUR PROTECTED HEALTH INFORMATION OR SPECIMEN(S):

Your information or samples collected for this study will NOT be used or shared for future research studies, even if we remove the identifiable information like your name, medical record number, or date of birth.

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 subject **Date**

_____
Printed name of research subject

_____ _____
Printed name of [authorized] person obtaining informed consent Date

_____ _____
Printed name of [authorized] person who reviewed the consent over the phone (if applicable) Date