

Document Coversheet

Study Title: Early reduction of Post-operative Pain and inflammation to Expedite Return to function after KNEE and SHOULDER arthroscopy (PROPER KNEE and SHOULDER Trial)

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	03/27/2023
NCT Number:	NCT05149287
IRB Number	63476
Coversheet created:	6/30/2023

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](#).

PROJECT INFORMATION

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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



Early reduction of Post-operative Pain and inflammation to Expedite Return to function after KNEE and SHOULDER arthroscopy (PROPER KNEE and SHOULDER Trial)

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.



PROPER

Anticipated Ending Date of Research Project:  1/1/2024

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

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

RISK LEVEL

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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.

Refer to [UK's guidance document](#) on assessing the research risk for additional information.



SUBJECT DEMOGRAPHICS

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

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](#)

This study will recruit a sample of 48 skeletally mature male and female participants between the ages of 18 and 55 that have undergone knee arthroscopy for the treatment of cartilage or meniscal pathology or shoulder arthroscopy for the treatment of rotator cuff injury. Participants will be recruited from the University of Kentucky's Department of Orthopaedic Surgery & Sports Medicine clinical patient population.

Complete subject inclusion and exclusion criteria are as follows, and patients will not be excluded on the basis of sex, race, or ethnicity:

Inclusion Criteria:

1. Written consent to participate in the study
2. Male or female greater than or equal to 18 years of age and less than 55 years of age
3. Is indicated for knee arthroscopy for cartilage or meniscal procedure OR shoulder arthroscopy for rotator cuff repair
4. Ambulatory and in good general health
5. Willing and able to comply with the study procedures and visit schedules and able to follow verbal and written instructions.
6. Willing to abstain from use of protocol-restricted medications during the study

Exclusion Criteria:

1. Known allergic reactions to cephalosporins
2. Reactive arthritis, rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, or arthritis associated with inflammatory bowel disease
3. History of infection in either knee/shoulder
4. Clinical signs and symptoms of active knee/shoulder infection or crystal disease in either knee/shoulder within 1 month of screening
5. Other surgery or arthroscopy of either knee/shoulder within 6 months of Screening
6. Intraarticular treatment of any joint with any of the following agents within three (3) months of Screening: any corticosteroid preparation or any biologic agent (e.g., platelet rich plasma (PRP) injection, stem cells, prolotherapy, amniotic fluid injection; investigational or marketed).
7. Intraarticular treatment in either knee/shoulder with hyaluronic acid (investigational or marketed) within 3 months of Screening
8. Parenteral or oral corticosteroids (investigational or marketed) within 3 months of Screening
9. Inhaled, intranasal or topical corticosteroids (investigational or marketed) within 2 weeks of Screening
10. Females who are pregnant or nursing or plan to become pregnant during the study; men whose female partner plans to conceive during the study
11. Radiographic osteoarthritic changes defined as Kellgren-Lawrence grade 2 or greater (as determined by PI from patient's preoperative X-rays)
12. Inability to read and understand English
13. Any prior diagnosis of antibiotic-resistant diarrhea

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:	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Asian:	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Black/African American:	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Latinx:	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Native Hawaiian/Pacific Islander:	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
White:	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
American				

Arab/Middle Eastern/North African:				
Indigenous People Around the World:				
More than One Race:				
Unknown or Not Reported:				

If unknown, please explain why:

It is not known at the time the demographics of the participants that will be recruited. This information will continue to be updated as study recruitment continues.

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)

ADDITIONAL INFORMATION:

- 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

Please visit the [IRB Survival Handbook](#) for more information on:

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

Other Resources:

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

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

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

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

Yes No

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

Examples of such conditions include:

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

Attachments

INFORMED CONSENT/ASSENT PROCESS/WAIVER

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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

Attach Type	File Name
Informed Consent/HIPAA Combined Form	Proper consent v15_cc.pdf

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](#).

CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent forms describing in detail the study intervention, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study intervention.

CONSENT PROCEDURES AND DOCUMENTATION

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Consent forms will be Institutional Review Board (IRB)-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

Participants are free to ask any question they may have about the study. Participants will be directed to contact the Principal Investigator or Study Coordinator if complaints, concerns, or questions arise. Participants will be provided with the Principal Investigator or Study Coordinator's name and current contact information at the time they are enrolled in the study and at the time of the informed consent process. Participants will also be advised to contact the staff of the Office of Research Integrity at 859-257-9428 or toll free at 1-866-400-9428 with any concerns.

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.

e) If the research involves using or accessing identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format.

- Private information/specimens are "identifiable" if the investigator may ascertain the identity of the subject or if identifiers are associated with the information (e.g., medical records). This could be any of the [18 HIPAA identifiers](#) including [dates of service](#).
- If not using identifiable private information or identifiable biospecimens, insert N/A below.

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

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

Select the option below that best fits your study.

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



Option 1

Describe how your study meets these criteria:

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

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

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

Option 2

Describe how your study meets these criteria:

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

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

Option 3

Describe how your study meets these criteria:

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

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

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

RESEARCH DESCRIPTION

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comment(s)

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

Pro Tips:

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

Background

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

Arthroscopic surgery for cartilage and meniscus injuries are some of the most common orthopaedic procedures currently performed. We and others demonstrated an increase in the proinflammatory environment of the knee following surgery. The effects of cartilage or meniscus injury increase the risk of developing post-traumatic osteoarthritis (PTOA) and subsequent total knee arthroplasty. Even surgical treatment alone does not eliminate PTOA risk, as the relative risk for PTOA after partial meniscectomy ranges from at least 2.7 to 14.0. Similar phenomena are observed in the shoulder following rotator cuff injuries. Studies have demonstrated increases in synovial inflammation and matrix metalloproteinases in those with full thickness rotator cuff tears. Additionally, OA is common following rotator cuff repairs, and a significant association has been observed between massive rotator cuff repairs and glenohumeral osteoarthritis. Despite these challenges, no disease modifying intervention exists to improve early pain and function. The long-term goal of this project is to control the early cerative inflammation state to reduce pain and opioid use, improve sleep quality, and reduce cartilage breakdown after knee or shoulder surgery.

Post-surgical pain is initiated through an inflammatory response to the insult of surgery. The pain response leads to sleep disruption and a further increase in pain and additional sleep disruption. Opioid medications are often used after surgery to treat pain despite the side effect profile. These medications also contribute to poor sleep quality and duration. Early pain and narcotic use can be controlled by mitigating the effects of post-surgical inflammation. The principal proinflammatory agent responsible for postoperative pain is prostaglandin E2 (PGE2). PGE2 is a product of the arachidonic acid (AA) pathway. Cyclooxygenase (COX)-1 or COX-2 converts AA to prostaglandin H2 (PGH2), and prostaglandin E synthase (PGES) transforms PGH2 to PGE2. Current NSAIDs either weakly inhibit both COX-1 and 2 or selectively inhibit COX-2. These medications have significant side effects by inhibiting the synthesis of all physiologically needed prostaglandins downstream of PGH2. Microsomal PGES-1 (mPGES-1), an inducible enzyme, is an ideal target for a next generation of anti-inflammatory drugs, because the mPGES-1 inhibition will only block the mPGES-1-associated over-production of PGE2 without affecting the production of other prostaglandins, as confirmed by reported mPGES-1 knock-out studies. Ceftriaxone, a readily available third generation cephalosporin antibiotics inhibits mPGES-1 and associated PGE2 production and is expected to have the desirable anti-inflammatory and analgesic effects of COX-1/2 inhibitors, but without the side effects caused by the COX-1/2 inhibition. Since it is highly selective in its inhibition, ceftriaxone is an excellent candidate for reducing immediate post-operative pain and heightened inflammatory response. Furthermore, injectable ceftriaxone with lidocaine is extensively used in routine practice, even used on children under two years old for antibiotic resistant ear infections.

We hypothesize that ceftriaxone will decrease post-operative pain surgery compared to placebo. We additionally hypothesize that the decreased pain and reduced postoperative inflammatory burden will result in decreased narcotic consumption and improved sleep quality thereby creating an optimal environment for recovery.

Objectives

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

Primary Objective: Determine if a one time postoperative dose of ceftriaxone reduces post-operative visual analog scale (VAS)-pain scores and narcotic consumption compared to placebo. Hypothesis: Ceftriaxone administration will improve VAS-pain scores by greater than 2 points during the early post-operative period and prevent break through narcotic consumption when compared to placebo.

Secondary Objective 1: Determine if ceftriaxone creates an optimal environment for healing by reducing the systemic inflammatory burden and improving sleep quality. Hypothesis: The Ceftriaxone group will demonstrate significantly lower concentrations of serum inflammatory markers, will be positively correlated with improved patient reported outcomes (PROs), early functional return, and serum inflammatory profiles at two months postoperative.

Secondary Objective 2: Determine if a one time postoperative dose of ceftriaxone reduces cartilage breakdown and the short-term inflammatory burden. Hypothesis: Ceftriaxone treatment will decrease urinary cartilage breakdown (as measured by C-terminal telopeptide-2 (CTX-2)).

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](#).

We will enroll 24 patients ages 18–55 years prior to undergoing knee arthroscopy for the treatment of cartilage or meniscal pathology and 24 patients ages 18–55 years prior to undergoing shoulder arthroscopy for the treatment of rotator cuff injury. Patients will be randomized to receive placebo or ceftriaxone the day of surgery. Those randomized to the ceftriaxone group will receive an intravenous injection immediately postoperative. The rationale for this is to examine the effects of a single post-operative dose, while decreasing the complexity and the risk profile to the patient. Randomization will be double blinded as placebo injections will be administered in the form of dilute lidocaine and saline. A joint aspiration of both the operative and nonoperative knees or shoulders will be also performed in the operating room on the day of surgery (Visit 2). We are collecting synovial fluid from the operative knee or shoulder to evaluate the inflammation level before study medication delivery. We are collecting fluid from the contralateral knee or shoulder as well to serve as a comparison to the operative knee or shoulder. Aspirations are done during surgery so that patients will be under anesthesia so they will not experience pain. Patients will be assessed at the first post-operative visit (5–12 days) and at 2 months. The primary outcome variable will be serum PGE2 levels. Initial serum samples will be drawn day of surgery and at 5–12 day post-operative visit. Secondary outcome measures include immediate post-operative narcotic use, sleep quality and activity, serum markers of inflammation, and patient reported outcomes at 2 months. VAS-Pain scores will be electronically assessed each week for 2 months. Post-operative narcotic use will be monitored with pill counts at the first post-operative visit. Sleep quality will be monitored through questionnaires and through an accelerometer. PROs will be collected at the pre-operative enrollment visit, 1 week, and 2 months. Serum proteomic analysis for the arachidonic acid and nuclear factor(NF)-KB pathways. Outcomes will be assessed through repeated measures multivariate analysis of variance and corrected student's t-test. In addition, to meet the request of the antibiotic stewardship committee, safety information and potential adverse events will be assessed 2, 7, and 14 days after surgery.

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](#)

This single site study will include 48 patients that have undergone knee arthroscopy for cartilage or meniscus procedures or shoulder arthroscopy for rotator cuff repair. Based on our current and recent randomized trials assessing interventions prior to or following knee arthroscopic procedures (ClinicalTrials.gov Identifiers: NCT02930122, NCT03364647, NCT03429140) we anticipate a similar rate of eligible patients that agree to participate in the current study (76%). Extrapolating from our annual patient volume and RCT agreement rate, we do not anticipate difficulty in enrolling 48 patients over an 8 month period. Furthermore, our established relationship with other clinicians, dedicated research personnel with dedicated research space in our clinical facility also support the feasibility of successfully completing the proposed project.

- **Accrual Rate:** Enroll 6 patients per month for 8 months
- Patients will be recruited from the outpatient clinical populations of the UK HealthCare sports medicine surgeons at the UK HealthCare Orthopaedic and Sports Medicine Center
- Potentially eligible patients will be identified by their surgeon during a regularly scheduled preoperative visit. Patients will then meet with a member of the research team to discuss the study, determine eligibility, and provide informed consent.
- No advertisement will be used for this study.
- Since study visits coincide with routine standard of care follow-up visits 1 and 8 weeks after surgery, patients will be reminded of their visit by the UKHealthCare automated phone reminder system. In addition, research personnel will contact patients via the patient's preferred method of contact (phone, text message, and/or email) 2 days prior to their visit to remind the patient of their upcoming visit.
- Caucasian patients account for 84% of our patient population; however, we take the inclusion of minorities very seriously. In a recently completed clinical trial of ACL reconstructed patients, our successful enrollment strategies have resulted in a greater representation of minorities than the general patient population for our area (29% vs. 16%). We aim to meet or exceed these proportions in the proposed study and will approach all eligible minority patients to ensure that at least 25% are non-white.

• Vulnerable populations including pregnant women, children, and prisoners will not be enrolled in this study.
No advertisements will be used for this study.

Attachments

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.

During standard of care follow up visits before surgery or on surgery day, patients will be asked to sign a consent form and perform screening related procedures. If patients choose to take part in this study, they will be randomly assigned to one of two study groups in a double-blinded fashion. One group will receive ceftriaxone and the other group will receive a placebo prepared by the investigational drug pharmacy. Randomization will occur through the use of a random number generator. Randomization of the drug will be performed at drug preparation in pharmacy. The list will be stored electronically. They will have equal chance of being in either group. A FitBit will be given to each participant at the time of enrollment. Participation in the study will take place in 4 visits, including the surgery day. Patients will receive either intravenous injections of lidocaine and ceftriaxone or injectable placebo consisting of saline and lidocaine once immediately following surgery. This dose will be observed in the PACU. All study visits will take place during normally scheduled surgery follow-up visits. Females who are able to become pregnant will undergo a urine pregnancy screen on their surgery day as part of standard of care. Active surveillance for multiple drug resistant organisms will be performed using nasal swabs pre-operatively at the final standard of care visit at 2 months.

Attachments**Data Collection & Research Materials**

In this section, please provide the following:

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

Post-operative narcotic use will be monitored with pill counts at the first post-operative visit. Sleep quality will be monitored through daily questionnaires and FitBit devices that will track daily rest/wake activity. PROs; including the Visual Analogue pain Scale (VAS), Knee injury and Osteoarthritis Outcome Score global (KOOSglobal) (for knee patients), American Shoulder and Elbow Surgeons (ASES) shoulder score (for shoulder patients), and the Regularity, Sleep Quality, Alertness, Timing, Efficiency, Duration scale for sleep (RU SATED); will be collected at the day of surgery, 1 week, and 2 months. Serum proteomic analysis for the arachidonic acid and nuclear factor(NF)- κ B pathways and will be processed through the Center of Biomedical Research Excellence (COBRE, NIH P20 GM130456) Computational Core. Outcomes will be assessed through repeated measures multivariate analysis of variance and corrected student's t-test.

Data will be collected using REDCap. REDcap is a secure, web-based program to capture and store data at the University of Kentucky.

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data.

Hardcopies of the study visit worksheets will be provided for use as source document worksheets for recording data for each participant enrolled in the study. Clinical data will be entered onto paper case report forms. Clinical data will be transcribed directly from the source documents.

Good clinical practice compliance monitoring to be performed by the PI with regular meetings and drug log.

Attachments

Attach Type	File Name
DataCollection	Sleep Diary.docx
DataCollection	ases shoulder score.pdf
DataCollection	KOOSglobal Questionnaire.pdf

DataCollection	RU Sated Scale Questions.docx
DataCollection	RU Sated 1.pdf
DataCollection	RU Sated 2.pdf

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.

Data collection will take place at the University of Kentucky's Orthopaedic and Sports Medicine Center and the Sports Medicine Research Institute. The participants will be followed by the principal investigator and their research team which includes physicians, certified nurses, and clinical research coordinators during the study. Emergency medical equipment, medications and supplies will be at the physician's disposal should the participant have an acute untoward reaction.

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.

Potential breach of confidentiality

KNOWN POTENTIAL RISKS OF INJECTABLE CEFTRIAXONE

The following risks are copied directly from the Rocephin (Injectable ceftriaxone) package insert:

ADVERSE REACTIONS: Rocephin is generally well tolerated. In clinical trials, the following adverse reactions, which were considered to be related to Rocephin therapy or of uncertain etiology, were observed:

LOCAL REACTIONS—pain, induration and tenderness was 1% overall. Phlebitis was reported in <1% after IV administration. The incidence of warmth, tightness or induration was 17% (3/17) after IM administration of 350 mg/mL and 5% (1/20) after IM administration of 250 mg/mL.

HYPERSENSITIVITY—rash (1.7%). Less frequently reported (<1%) were pruritus, fever or chills.

HEMATOLOGIC—eosinophilia (6%), thrombocytosis (5.1%) and leukopenia (2.1%).

Less frequently reported (<1%) were anemia, hemolytic anemia, neutropenia, lymphopenia, thrombocytopenia and prolongation of the prothrombin time.

GASTROINTESTINAL—diarrhea (2.7%). Less frequently reported (<1%) were nausea or vomiting, and dysgeusia. The onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment (see WARNINGS).

HEPATIC—elevations of SGOT (3.1%) or SGPT (3.3%). Less frequently reported (<1%) were elevations of alkaline phosphatase and bilirubin.

RENAL—elevations of the BUN (1.2%). Less frequently reported (<1%) were elevations of creatinine and the presence of casts in the urine.

CENTRAL NERVOUS SYSTEM—headache or dizziness were reported occasionally (<1%).

GENITOURINARY—moniliasis or vaginitis were reported occasionally (<1%).

MISCELLANEOUS—diaphoresis and flushing were reported occasionally (<1%). Other rarely observed adverse reactions (<0.1%) include leukocytosis, lymphocytosis, monocytosis, basophilia, a decrease in the prothrombin time, jaundice, gallbladder sludge, glycosuria, hematuria, anaphylaxis, bronchospasm, serum sickness, abdominal pain, colitis, flatulence, dyspepsia, palpitations, epistaxis, biliary lithiasis, agranulocytosis, renal precipitations, and nephrolithiasis.

There are also theoretical risks of clostridium difficile infection and promotion of antibiotic resistance.

The risks of the study, which include the known risks associated with ceftriaxone and the risks associated with intramuscular injection, are outweighed by the potential benefits. Patients in both the experimental and placebo groups have the potential benefit of pain relief, and there may also be a potential chondroprotective benefit of the study drug. As such, the risks of participation in the study outweigh the value of the information to be gained.

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).

If the participant does not want to take part in the study, they can receive their normal (standard) care after knee or shoulder surgery. They will be advised to discuss these treatment options with their doctor.

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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](#)

The investigative team maintains the right to keep, preserve, use and dispose of the findings of this investigation in accordance with Food and Drug Administration (FDA) guidelines. The FDA maintains the right to inspect the records of the study at any time. Investigational records from this study will be maintained in a confidential manner; participant names will not be associated with any published results.

Biomarker analyses will be performed at the study conclusion and we do not anticipate clinically relevant findings at that time. The biomarkers under investigation are not diagnostic and would not provide clinically relevant information. Since this is post operative, all standard of care work-up would have been met (MRI, etc).

Patient demographics will be recorded from AEHR, all outcomes will be collected in REDcap.

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and their interventions. This confidentiality is extended to cover testing of biological samples in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the investigator.

All research activities will be conducted in as private a setting as possible.

The CCTS QA/QI auditor, representatives of the Institutional Review Board (IRB), regulatory agencies or pharmaceutical company supplying study product may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. It will be stored in the room 1620 of the Turfland Clinic at 2195 Harrodsburg Road, Lexington, KY 40504. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at the University of Kentucky. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by University of Kentucky, Department of Orthopaedic research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the University of Kentucky.

Data will be collected and stored in REDcap. Data will be maintained for 7 years, then destroyed per university policy.

Every precaution to prevent a direct study injury will be taken by medical personnel and the investigators. Should an adverse or serious adverse event occur, the research participant will be followed by physicians, registered nurses and other research staff members for the duration of the participant's hospitalization. In addition study will be paused pending IRB review of any discovered incidence of antibiotic-resistant diarrhea. Routine care will be provided by hospital staff. Emergency medical equipment, medications and supplies will be at the physician's disposal should the participants have an acute untoward reaction.

Furthermore, in response to consultation by the antibiotic stewardship team, we have implemented strict measures and reporting of AEs. The plan will be to have 3 contacts with participants within the first 2 weeks after surgery (2, 7, and 14 days after surgery) with a minimum of 1 of the 3 visits being an in-person evaluation and the other two being by the patient's preferred method of contact (phone, text, or email).

Specific questions asked to monitor AE's will be:

1. Do you have any redness around the knee or shoulder?
2. Have you noticed any discolored drainage from your surgical incisions?
3. Have you been feeling sick or ill? If so, what symptoms have you had?
4. Have you noticed a generalized rash since receiving the study drug?
5. Have you experienced diarrhea?

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

Yes No

Payment

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

Patients will receive \$20 by check after completion of the final follow-up visit.

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 will be no added cost to participants due to procedures carried out purely for research purposes. Patients are still responsible for costs that are considered medically necessary and would be part of the care they receive even if they do not take part in this study. The University of Kentucky is not allowed to bill patients or insurance companies for the medical procedures done strictly for research.

Therefore, these costs will be paid by the study

- Administration of the study medication
- All questionnaires collected at Visits 1,3, and 4
- Blood draws at visits 1 and 2
- Synovial fluid aspirations at visit 2
- Nasal swabs at visits 1 and 4

Data and Safety Monitoring

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

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

Data and Safety Monitoring Plan: Monitoring for adverse events will be conducted in real-time by the study investigators and study coordinators. Risks involved with this study are considered greater than minimal risk. Patients will be clinically seen by their surgeon multiple times per their routine standard of care postoperative follow-up schedule (Standard of care visit schedule: 1-2 weeks after surgery, and then 2 months). If an AE (either listed above or any untoward event) is reported to the research personnel at any of the time points the PI is immediately notified. Additionally all AEs will be reported to the IRB in accordance with the set time guidelines.

Safety will be monitored: The plan will be to have 3 contacts with participants within the first 2 weeks after surgery (2, 7, and 14 days after surgery) with a minimum of 1 of the 3 visits being an in-person evaluation and the other two being by the patient's preferred method of contact (phone, text, or email). A member of the research team will be responsible for contacting the patients at each time point and documenting the responses to the following questions.

Specific questions asked to monitor AE's will be:

1. Do you have any redness around the knee or shoulder?
2. Have you noticed any discolored drainage from your surgical incisions?
3. Have you been feeling sick or ill? If so, what symptoms have you had?
4. Have you noticed a generalized rash since receiving the study drug?
5. Have you experienced diarrhea?

To ensure completion of the required documents we have adverse event data collection instruments scheduled in our REDCap project at each data collection time point in which the coordinator documents the AE information and the action taken. These instruments are completed as any other CRF with the study and are a source of data retention. In addition to completing these instruments, there is a prompt in the instrument to remind the research staff to review the IRB submission guidelines to ensure AEs are reported in a timely manner. Lastly, we have implemented weekly study meetings with all research personnel in which the study activities (routine: ie scheduled follow ups or unexpected: ie adverse events) are reviewed to ensure all appropriate actions have been taken for the study.

Study Stopping Criteria:

1. Sign of allergic response to Ceftriaxone
2. Any patient reported and drug related SAE after the administration of the study drug.

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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

We will store, use and share coded biological samples and biomarker data for future research. These samples can be used to research the causes of osteoarthritis after meniscus or rotator cuff injury, its complications and other conditions for which individuals with meniscus, knee cartilage or rotator cuff injuries are at increased risk, and to improve treatment. No genetic testing will be performed on these stored samples. The information will be stored at the university of Kentucky orthopedic biomarker repository indefinitely. We will take careful steps to keep your information confidential. We will remove direct identifiers from information or samples. We will label information or samples with a code and will store the key separately from the master code list. Only select staff will have access to the list that links the code to the subject.

We will store samples in a locked freezer that is located behind locked. We will store identifiable information, in a, password-protected database; encrypted file which changes it to another format to protect it from being accessed by anyone outside of the approved staff. The staff follow procedures to keep subject identity a secret to the extent allowed by law. In very unusual cases, staff may be required to release identifiable medical and research information in response to an order from a court of law. Officials of the Food and Drug Administration, the University of Kentucky and The UK Center for Clinical and Translation Science may look at or copy pertinent portions of records that identify the subject. The subjects de-identified information or samples may be shared with other researchers without additional informed consent, provided an Institutional Review Board (IRB) has approved this action.

A researcher who receives information or specimens will sign an agreement to use the data responsibly. We will destroy any remaining information and samples that have been stored. In addition, it may be possible to destroy the code that links the subject with specimen samples. However, we cannot withdraw the information and samples that have already been used.

The subject may withdraw permission to allow their information or samples to be used for future research. To do so, they must send a written withdraw request to:

Austin Stone, MD

Department of Orthopaedic Surgery & Sport Medicine 740 S Limestone, Suite K401
Lexington, KY 40536-0284

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**

Yes No

HIV/AIDS Research

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

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

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

PI-Sponsored FDA-Regulated Research

Is this an investigator-initiated study that:

- 1) involves testing a Nonsignificant Risk (NSR) Device, or
- 2) is being conducted under an investigator-held Investigational New Drug (IND) or Investigational Device Exemption (IDE)?

Yes No

PI-Sponsored FDA-Regulated Research

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

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

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

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 NoIf yes, complete the questions below. Additional [study drug guidance](#).

LIST EACH DRUG INVOLVED IN STUDY IN THE SPACE BELOW

Drug Name:

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:

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. 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	Ceftriaxone Study Drug Form_updated.pdf
Study Drug Form	Placebo Study Drug Form_updated.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 regular 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:

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

Attachments

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

- Academic Degree/Required Research
- Alcohol/Drug/Substance Abuse Research
- Biological Specimen Bank Creation (for sharing)
- Cancer Research
- CCTS-Center for Clinical & Translational Science
- Certificate of Confidentiality
- Clinical Research
- Clinical Trial - Phase 1
- Clinical Trial
- Collection of Biological Specimens for internal banking and use (not sharing)
- Community-Based Participatory Research
- Deception
- Educational/Student Records (e.g., GPA, test scores)
- Emergency Use (Single Patient)
- Gene Transfer
- Genetic Research
- GWAS (Genome-Wide Association Study) or NIH Genomic Data Sharing (GDS)
- Human Cells, Tissues, and Cellular and Tissue Based Products
- Individual Expanded Access or Compassionate Use
- International Research
- Planned Emergency Research Involving Exception from Informed Consent
- Recombinant DNA
- Registry or data repository creation
- Stem Cell Research
- Suicide Ideation or Behavior Research
- Survey Research
- Transplants
- Use, storage and disposal of radioactive material and radiation producing devices
- Vaccine Trials

For additional requirements and information:

- [Cancer Research \(MCC PRMC\)](#)
- [Certificate of Confidentiality](#) (look up "Confidentiality/Privacy...")
- [CCTS \(Center for Clinical and Translational Science\)](#)
- [Clinical Research](#) (look up "What is the definition of...")
- [Clinical Trial](#)
- [Collection of Biological Specimens for Banking](#) (look up "Specimen/Tissue Collection...")
- [Collection of Biological Specimens](#) (look up "Specimen/Tissue Collection...")
- [Community-Based Participatory Research](#) (look up "Community-Engaged...")
- [Data & Safety Monitoring Board](#) (DSMB)

*For Medical IRB: [Service Request Form](#) for CCTS DSMB

- [Data & Safety Monitoring Plan](#)
- [Deception*](#)

*For deception research, also go to the E-IRB Application Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"

- [Emergency Use \(Single Patient\) \[attach Emergency Use Checklist\]](#) (PDF)
- [Genetic Research](#) (look up "Specimen/Tissue Collection...")
- [Gene Transfer](#)
- [HIV/AIDS Research](#) (look up "Reportable Diseases/Conditions")
- [Screening for Reportable Diseases \[E2.0000\]](#) (PDF)
- [International Research](#) (look up "International & Non-English Speaking")
- [NIH Genomic Data Sharing \(GDS\) Policy](#) (PDF)
- [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"

- [Use, storage and disposal of radioactive material and radiation producing devices](#)

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:

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.):

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](#)

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](#)

The research involves use of Department of Defense (DoD) funding, military personnel, DoD facilities, or other (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.

63476 Statistical Analysis Plan:

Primary objective will be assessed using two-tailed independent t-tests for comparison between timepoints. Similarly, all secondary measures will be assessed using two-tailed independent t-tests.