Study Protocol and Statistical Analysis Plan

Effect of All-Stim 2 Quadriceps Treatments on Limb Muscle Strength In Mechanically Ventilated Patients

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Consent to Participate in a Research Study: Effect of All-Stim 2 Quadriceps Treatments on Limb Muscle Strength In Mechanically Ventilated Patients

WHY ARE YOU BEING INVITED TO TAKE PART IN THIS RESEARCH?

You are being asked to participate in the research study at the University of Kentucky to determine if administration of All Stim 2 stimulator treatments can improve leg muscle strength in critically ill patients. You will be one of 24 patients asked to participate in the study.

Because of your condition, you may not be able to make the decision to participate in this research. In this case,_____, your legally authorized representative will attempt to decide what you would do if you were able to choose whether or not to be in this study. Your legally authorized representative will determine whether your participation in this study is in your best interest.

WHO IS DOING THE STUDY?

The person in charge of the study is Dr.Gerald Supinski of the University of Kentucky, Department of Medicine. There may be other people on the research team assisting at different times during the study.

WHAT IS THE PURPOSE OF THIS STUDY?

Patients that are on mechanical ventilators in medical intensive care units have extremely weak leg muscles. Currently there is no treatment to prevent or reverse this weakness. Treatments with a thigh muscle stimulator, called an All Stim 2, can improve leg muscle strength and help patients regain leg function after knee surgery. The purpose of the present study is to determine if treatments with All Stim 2 device can also improve leg muscle strength in patients on mechanical ventilation.

ARE THERE REASONS WHY YOU SHOULD NOT TAKE PART IN THIS STUDY?

If you have a pacemaker or implanted defibrillator you cannot participate in this study.

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

These studies will be conducted at the University of Kentucky hospital. The study will take 8 days; in addition, Dr Supinski or Dr. Callahan will visit you on day 28 to assess your ability to walk and to ask you questions about your health status.

WHAT WILL YOU BE ASKED TO DO?

We will first measure the strength of your leg muscles. We will then place All Stim 2 devices on your thigh muscles for 30 minutes a day for 7 days. On day 8, leg muscle strength will be reassessed.

To measure right leg muscle strength, we will place a force detector around the right lower leg and stimulate a muscle in the right thigh called the quadriceps muscle (muscle of the front of your thigh). Stimulation will be performed using a magnetic coil placed over the nerve to the quadriceps. We will measure muscle strength three times and then remove the force detector. We will then repeat these measurements on the left side to assess left thigh muscle strength.

The All Stim 2 regimens to be used are provided below. You will receive one of two regimens; the choice as to which you will get will be determined randomly. One patient will be placed into the placebo treatment group (point 1 next) for every two patients placed into the active treatment group (point 2 next). As a result, you have a I out of 3 chance of receiving placebo treatment and a 2 out of 3 chance of receiving active treatment.

(1)Placebo treatments; for these treatments All Stim 2 electrodes will be placed on both the right and left thighs for 30 minutes each day; the stimulator currents will be set to zero power levels so that no actual stimulation is provided. This treatment will be continued for 7 days.

(2)Active treatments; for these treatments All Stim 2 stimulators will be placed on both the right and left thighs for 30 minutes each day; the stimulator currents will be set to power levels of 60-80 on each side for the 30 minute period. This level of stimulation should result in bilateral muscle contractions for a 30 minute period. This treatment will be continued for 7 days.

On day 8 we will repeat measurements of right and left leg muscle strength using the magnetic twitch technique described above.

On day 28 Dr. Supinski and/or Dr. Callahan will visit you and ask you to walk for 6 minutes to see how far you can walk in that time. In addition, they will administer the St. Georges Research Questionnaire; as part of this assessment they will ask you to tell them information about how well you feel and if you are capable of performing activities of daily living.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

You are not a candidate for these measurements if you have a pacemaker or implanted defibrillator since electrical and magnetic pulses can affect pacemaker and defibrillator function.

There have been no reported instances of side effects or complications from leg strength measurements using magnetic stimulators in patients without pacemakers. While there are no major risks to the performance of these measurements, there may be a sensation of muscle contraction from magnetic stimulation of the nerves to the leg muscles. The magnetic stimulation will create the sensation of muscles contracting in the leg; this sensation will only last for a second after the magnet is activated.

Use of the All Stim 2 device will create the sensation of a tingling feeling in the thigh muscle. Removal of the All Stim 2 unit may pull on your thigh hair. If you have very hairy thighs, we will either shave the thigh or use Nair hair removal treatment to remove the hair.

In addition to the risks listed above, you may experience a previously unknown risk or side effect. As a result, a physician will be in attendance at all times during the study and will stop measurements if any harmful effects are observed.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

If the All Stim 2 unit improves your strength, it may help you recover from your illness faster and have better long term exercise tolerance. Since this is the first time this device has been tested in critically ill patients, however, there is no guarantee that it will improve your strength. In addition to a potential benefit to you, your willingness to take part in this study may help doctors better understand and/or treat others who have your condition.

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 decide not to take part in this study, your decision will have no effect on the quality of medical care you receive.

IF YOU DON'T WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?

There is currently no exercise therapy that is being used in the University of Kentucky MICU to prevent or reverse weakness in critically ill patients and if you do not participate in this study you will receive passive range of motion treatments by physical therapy, which is the standard care at this time.

WHAT WILL IT COST YOU TO PARTICIPATE?

The University of Kentucky will not bill your insurance company, Medicare or Medicaid for any of the medical procedures done in this study.

You and/or your insurance company, Medicare or Medicaid will be responsible for the costs of all care and treatment you receive during this study that you would normally receive for your condition. These are costs that are considered medically reasonable and necessary and will be part of the care you receive if you do not take part in this study.

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

We will 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. You will not be personally identified in these written materials. We may publish the results of this study; however, we will keep your name and other identifying information private.

We will 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. The records for this study will be kept in a locked file cabinet to which only Dr. Supinski and Dr. Callahan have access.

Officials from the University of Kentucky and FDA may look at or copy pertinent portions of records that identify you.

CAN YOUR TAKING PART IN THE STUDY END 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. The individuals conducting the study may need to withdraw you from the study. This may occur if you are not able to follow the directions they give you or if they find that your being in the study is of more risk than benefit to you. If you withdraw or are withdrawn from the study the study treatment will no longer be provided and may not be available.

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

You may take part in this study if you are currently involved in another research study. 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 Dr. Supinski at 859-494-3480 immediately. Dr. Supinski 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. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study.

The medical costs related to your care and treatment because of research related harm will be your responsibility. You do not give up your legal rights by signing this form.

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

You will not receive any rewards or payment for taking part in the study.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS, CONCERNS, OR COMPLAINTS?

Before you decide whether to accept this invitation to take part in the study, please ask any questions that might come to mind now. Later, if you have questions, suggestions, concerns, or complaints about the study, you can contact the investigator, Dr. Gerald Supinski at 859-494-3480. If you have any questions about your rights as a volunteer in this research, contact the staff in the Office of Research Integrity at the University of Kentucky at 859-257-9428 or toll free at 1-866-400-9428. We will give you a signed copy of this consent form to take with you.

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

If the researcher learns of new information in regards to this study, and it might change your willingness to stay in this study, the information will be provided to you. You may be asked to sign a new informed consent form if the information is provided to you after you have joined the study.

WHAT ELSE DO YOU NEED TO KNOW?

This study is being financially supported by funds from the University of Kentucky

_____ _____

Signature of person agreeing to take part in the study Date

or the legally authorized individual

_____

Printed name of person agreeing to take part in the study

or the legally authorized individual

_____

Relationship of the legally authorized individual to the subject

_____ _____

Name of [authorized] person obtaining informed consent Date

_____

Signature of Investigator

Statistical Analysis Plan

T tests will be used to compare variables (e.g. force) before and after physical therapy, with post-hoc testing (Tukeys) to determine differences. A p value of less than 0.05 will be taken as indicating statistical significance for comparisons.

PROTOCOL TYPE

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Which IRB

◉ Medical ○ NonMedical

Protocol Process Type

○ Exemption
○ Expedited (Must be risk level 1)
◉ Full

IMPORTANT NOTE: Once you have saved your choices under "Which IRB" and "Protocol Process Type", you will not be able to change your selections. If you select the wrong IRB Type and/or your application is deemed eligible for a different Protocol Process Type, it may be necessary to create a new application.

Please see below for guidance on which selections to make, and/or go to ORI's "Getting Started" web page. If you still have questions about which IRB or Protocol Process Type to choose, please contact the Office of Research Integrity (ORI) at 859-257-9428 **prior** to saving your selections.

Which IRB

The **Medical IRB** reviews research emanating from the Colleges of Dentistry; Health Sciences; Medicine; Nursing; Pharmacy and Health Sciences; and Public Health.

The **Nonmedical IRB** reviews research originating from the Colleges of Agriculture; Arts & Sciences; Business & Economics; Communication & Information; Design; Education; Engineering; Fine Arts; Law; and Social Work. The Nonmedical IRB does not review studies that involve administration of drugs, testing safety or effectiveness of medical devices, or studies that involve invasive medical procedures, regardless of from what college the application originates.

Which Protocol Process Type

Under federal regulations, an investigator's application to conduct a research project involving human subjects can be processed by the IRBs in three ways:

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

The preliminary determination that a research project is eligible for exemption certification or expedited review is made by the investigator. For assistance in determining which review process type your IRB application is eligible for, please go to ORI's "Getting Started" web page.

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.

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

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:
24

Enter the number of enrolled subjects (or records/specimens reviewed) that **have not been previously reported** to the IRB
0

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:
15

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

15

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)

Our records for the previously approved IRB application indicate:

This **study is monitored** by a Data and Safety Monitoring Board (DSMB): **N**

There is a Data and Safety Monitoring Plan: **Y**

If yes, to any of the above, 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:

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

- (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:

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:

12/30/2021

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
Callahan	Leigh Ann

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.

We have stopped recruitment because of COVID-19 and are waiting for this pandemic to subside before recruiting additional patients.

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.):

No new modifications.

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:

Ethnic Origin	#Male	#Female
American Indian/Alaskan Native:	0	0
Asian:	0	0
Black/African American:	0	0
Hispanic/Latino:	0	0
Native Hawaiian/Pacific Islander:	0	0
White/Caucasian:	4	11
Other or Unknown:	0	0

If unknown, please explain why:

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:

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.

If applicable, submit one copy of the entire **signed HIPAA Authorization form** for the same last TWO subjects enrolled.

Attachments

PROJECT INFORMATION

0 unresolved comment(s)

Title of Project: (If applicable, use the exact title listed in the grant/contract application). *** Effective 4/16/2020: If your research involves investigating any aspect of COVID-19, please enter "COVID19" at the start of your Project and Short Titles ***

Effects of All-Stim 2 Quadriceps Treatments on Limb Muscle Strength in Mechanically Ventilated Patients

Short Title Description

Note: "Short Title" should consist of a couple key words to easily identify your study - these key words (rather than the whole title) will be displayed on the Dashboard in the listing for your study.

Effects of All-Stim 2 Quadriceps Treatments on Lim

Anticipated Ending Date of Research Project: 12/30/2021

Number of human subjects (or records/specimens reviewed): 24

Study is/will be open to new subject enrollment or data/specimen collection: (•) Yes ( ) No

PI CONTACT INFORMATION

0 unresolved comment(s)

The Principal Investigator's (PI) contact information is filled in automatically based on who was logged in when the application was created (with LinkBlue ID). 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 the same person listed below.

If you are not the Principal Investigator, do NOT add yourself as study personnel. You may change the PI contact information on an application that is in Researcher edit mode by:

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

You will automatically be added as study personnel with edit authorization so you can continue editing the application.

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.

Note: 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*).

Change Principal Investigator:

First Name:	Gerald	Room# & Bldg:	L543, KY Clinic
Last Name:	Supinski	Speed Sort#:	405360284
Middle Name			
Department:	Internal Medicine - 7H350	Dept Code:	7H350
PI's Employee/Student ID#:	10241718	Rank:	Professor
PI's Telephone #:	859-323-0688	Degree:	MD
PI's e-mail address:	gerald.supinski@uky.edu	PI's FAX Number:	
PI is R.N.	○ Yes ◉ No	Trained:	Yes
		Date Trained	12/15/2018

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 [45 CFR 46.102(i)]

Download UK's guidance document on assessing the research risk for additional information on risk [PDF]

SUBJECT DEMOGRAPHICS

0 unresolved comment(s)

Age level of human subjects: (i.e., 6 mths.; 2yrs., etc..) 18 years to 80 years

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):

Enter Numbers Only!

Ethnic Origin	#Male	#Female
American Indian/Alaskan Native:		
Asian:		
Black/African American:	1	1
Hispanic/Latino:		
Native Hawaiian/Pacific Islander:		
White/Caucasian:	7	15
Other or Unknown:		

If unknown, please explain why: This projection is based on the number of patients recruited to date (15) with extrapolation to inclusion of an additional 9 patients over the remainder of the year.

Indicate the categories of subjects and controls to be included in the study. Depending on the subject category applicable to your research you may be required to complete additional forms. [Note, if the study does not involve direct intervention or direct interaction with subjects, (e.g., record-review research, outcomes registries), do not check mark populations which the research does not specifically target. For instance, a large record review of a diverse population may incidentally include a prisoner or an international citizen, but, if the focus or intent of the study has nothing to do with that status, you do not need to check those category(ies).]

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

ADDITIONAL INFORMATION:

☐ Children (individuals under age 18)

Please visit the IRB Survival Handbook under the named topic:

- ☐ 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

- Children/Emancipated Minors
- Students as Subjects
- Prisoners
- Impaired Consent Capacity Adults: Link to required Form

And/Or:

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

The next questions involve assessment of the study relative to 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). (you will not need to answer the impaired consent capacity questions)

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

◉ Yes ○ No

If Yes, go to the following link and complete and attach the indicated form unless you are filing for an exemption certification: https://ris.uky.edu/ori/oriforms/formt/Scale.asp

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

Attach Type	File Name
ImpairedConsent	Form_T_2Cii.doc

INFORMED CONSENT/ASSENT PROCESS/WAIVER

0 unresolved comment(s)

For 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 revise to be in accord with your research project.

Additional Resources:

- Sample Repository/Registry/Bank Consent (Word)
- Instructions for Proposed Informed Consent Document
- Instructions for Proposed Assent Form

Consent/Assent Tips:

- **If you have multiple consent documents, be sure to upload each individually (not all in a combined file).**
- **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**
  - **"Sponsor's Sample Consent Form".**

How to Get the Informed Consent Section Check Mark

1. **You must check the box for at least one of the consent items and/or check mark one of the waivers, then if applicable attach the corresponding document(s) as a PDF (if open to enrollment).**
2. **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 check mark the "Stamped Consent Doc(s) Not Needed".**
3. **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)
- ☐ Assent Form
- ☐ Cover Letter (for survey/questionnaire research)
- ☐ Phone Script
- ☐ Informed Consent/HIPAA Combined Form
- ☐ Debriefing and/or Permission to Use Data 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
Assent	Consent Form All Stim 2 for 2017.pdf
Informed ConsentParental Permission	Consent Form All Stim 2 for 2017.pdf

☐ Request for Waiver of Informed Consent Process

If you are requesting IRB approval for waiver of the requirement for the informed consent process, or alteration of some or all of the elements of informed consent (i.e. medical record review, deception research, or collection of biological specimens), 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 waiver of the requirement for the informed consent process.

☐ I am requesting 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.

The IRB may consider your request provided that **all** of the following conditions apply to your research and are appropriately justified. Explain in the space provided for each condition how it 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 Documentation of Informed Consent Process

If you are requesting IRB approval for waiver of the requirement for documentation of informed consent (i.e. telephone survey or mailed survey, internet research, or certain international research), **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 (i.e., 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 (i.e. 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, and 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, and explain in the space provided how your study meets the criteria for the selected regulatory option.

Note: The IRB cannot waive the requirement for documentation or alter the consent form for FDA-regulated research unless it meets Option #2 below. FDA does not accept Option #1.

Note: Even if a waiver of the requirement for documentation is approved by the IRB, participants must still be provided oral or written (e.g., cover letter) information including all required and appropriate elements of consent so they have the knowledge and opportunity to consider whether or not to participate. To help ensure required elements are included in your consent document, please use the **Cover Letter Template** as a guide: *English*- [WORD], Spanish- [WORD] The cover letter template was developed specifically for survey/questionnaire research; however, it may be useful as a guide for developing a consent document for other types of research as well.

Option 1

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

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

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 save by hitting 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 being completed to meet the requirements of a University of Kentucky academic program, the faculty advisor is also considered study personnel and should be listed as such below. ***Residents and students who are PI's are encouraged to designate at least one other individual (e.g., faculty advisor) 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 applicable personnel first, then click "select" by the listing for the person you want to add as study personnel to your protocol. For each individual selected, be sure to specify responsibility in the project, whether authorized by the principal investigator to obtain informed consent, AND denote who should regularly receive E-IRB notifications.

NOTE: Study personnel are required to receive human research protection (HSP) training before implementing any research procedures (e.g., CITI). For information about mandatory training requirements for study personnel, visit UK's FAQ's on Mandatory Training web 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 (Jen.Hill@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	Removed?	Last Updated	SFI
Callahan	Leigh Ann	Co-Investigator	SP	Y	N	MD	P	Y	11/15/2018	N	04/24/2018	N

RESEARCH DESCRIPTION

0 unresolved comment(s)

****!!!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: Provide an introduction and background information. Describe past experimental and/or clinical findings leading to the formulation of your study. For research involving investigational drugs, describe the previously conducted animal and human studies. You may reference grant application/sponsor's relevant protocol pages and attach as an appendix in the E-IRB "Additional Information" section, however, a summary paragraph must be provided in the text box below. For research that involves FDA approved drugs or devices, describe the FDA approved uses of this drug/device in relation to your protocol. Attach a copy of the approved labeling as a product package insert or from the Physician's Desk Reference in the applicable E-IRB "Study Drug" or "Study Device" section.

Introduction
I should point out that we are requesting a renewal for a previously approved protocol. We have recruited 15 patients to date and plan to finish this study by the end of the next review cycle. All the following information was included in the original Form B of the approved protocol.

Background.
Over the past 20 years there has been a dramatic growth in the numbers of patients requiring mechanical ventilation to sustain life in the United States. At most large medical centers, the number of patients needing more than transient mechanical ventilation for respiratory insufficiency has approximately tripled over the past 10 years. To deal with this burgeoning number of mechanically ventilated patients, stand-alone "ventilator: units have been created in the United States in most large cities, with literally hundreds of mechanically ventilated patients placed in such units in each of the large metropolitan areas in this country. In aggregate, we estimate that as many as 50,000 patients are on sustained mechanical ventilation at any given point in time in the United States, with a total of 600,000 patients/year requiring this form of treatment. The total cost of caring for these patients now consumes approximately 6% of the yearly health care budget, or upwards of 1% of the United States GNP (up to $150 billion dollars).

We are in the process of completing a study at the University of Kentucky that indicates critically ill patients have severe respiratory and limb muscle weakness. To date, this work has found that the average patient in the University of Kentucky MICU has a diaphragm pressure generation (Pdi) in response to phrenic magnetic twitch stimulation of only 8.5 + 3 cm H2O, compared to a normal value of 36 cm H2O for healthy adults. As a result, these patients have an average diaphragm strength that is only 24% of normal. In addition, we measured the strength of the largest leg muscle, the quadriceps in the thigh, and found that this muscle only generates an average twitch force of 12 + 4 Newtons in mechanically ventilated patients, compared to an average value of 38 Newtons for healthy adult controls. As a result, the leg strength of these patients is only 32% of normal. Our work also indicates that weakness is correlated with poor outcomes, with the weakest patients having the highest mortality, the longest duration on mechanical ventilation, and the longest ICU stays. Importantly, we found that weakness was a better predictor of patient outcomes than indices of lung disease (PaO2/FiO2 ratios, lung compliance, airway resistance), with weak patients having the same poor outcomes whether they have near normal or severe lung function. In addition, recent work by Dr. Herridge has shown that leg muscle weakness can persist for as long as five years after ICU discharge, with this prolonged weakness contributing greatly to long term morbidity and disability (1, 2).

Unfortunately, there is currently no specific defined treatment to prevent or reverse muscle weakness in mechanically ventilated patients. Some recent work suggests that vigorous physical therapy, involving cycling exercise of ICU patient, may improve outcomes (3). Such treatments are labor intensive, however, and few ICU's currently have the manpower or equipment to provide such treatments. In addition, many MICU patients require significant sedation and are too obtunded to realistically participate in any active exercise training regimen. In the University of Kentucky MICU patients are supposed to receive 3 treatments of passive range of motion by physical therapists a week, but compliance with this regimen is poor and only a small minority of patients receive even this modest level of therapy. This minimal level of physical exercise for bed bound ICU patients is typical for patients across the country, with the result that many patients who walk into hospitals need to leave in wheel chairs. Depending upon their health insurance status, some of these patients receive outpatient rehabilitation, but many receive little or no therapy even after hospital discharge.

Recently, a number of companies have developed electrical stimulation devices that can exercise the quadriceps, the major leg muscle, by stimulating this muscle to rhythmically contract. This newer technology represents an advance over older electrical stimulators which can be extremely painful and produce potentially injurious robot-like muscle contractions. Currently this technique is being used to provide rehabilitation to leg muscles after knee surgery in orthopedic patients. The purpose of the present study is to use one of these newer stimulators, the All-Stim 2, in mechanically ventilated MICU patients to provide a means of safely, nonvolitionally exercising the leg muscles of these patients. We postulate that this form of treatment will increase leg muscle strength in these patients, reduce the duration of hospitalization, improve long term mobility, and reduce indices of long term disability.

Objectives: List your research objectives. You may reference grant application/sponsor's relevant protocol pages and attach as an appendix in the E-IRB "Additional Information" section, however, a summary paragraph must be provided in the text box below.

The objective for this study is to determine if daily exercise using All-Stim 2 stimulation of quadriceps muscles will increase leg strength and improve outcomes (duration of hospitalization, long term mobility, long term disability) for mechanically ventilated MICU patients. We plan to randomize patients accepted into this protocol to administration of either sham exercise (i.e. placement of All-Stim 2 units on the legs for 30 minutes a day without activation of the electrical stimulation program) or active exercise (placement of All-Stim 2 electrodes on both legs and stimulating quadriceps muscles to rhythmically contract for 30 minutes a day). The two groups (sham and active exercise) will be treated for 30 minutes a day for seven days. The effects of exercise on quadriceps strength will be assessed by measuring quadriceps force generation (QuadTw) in response to magnetic stimulation of the femoral nerves. The QuadTw assessment will be made immediately before institution of sham or active exercise and will repeated one day after the conclusion of the seven day training regimen. Chart review and patient follow-up will be used to determine if this treatment regimen has an impact on clinical outcome measures, i.e. duration of hospitalization, long term mobility, long term disability.

Study Design: Describe the study design (e.g., single/double blind, parallel, crossover, etc.). Indicate whether or not the subjects will receive placebo medication at some point in the research procedures. Also, indicate whether or not the subjects will be randomized in this study. You may reference sponsor's protocol pages and attach as an appendix in the E-IRB "Additional Information" section, however, a summary paragraph must be provided in the text box below. (Including the study design table from a sponsor's protocol is helpful to IRB members.)

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.

Research Repositories: If the purpose of this submission is to establish a Research Repository (bank, registry) indicate whether the material you plan to collect would or would not be available from a commercial supplier, clinical lab, or established IRB approved research repository. Provide scientific justification for establishment of 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 [PDF] or the UK Research Registry Guidance [PDF]

The basic study design is to:
(a) obtain informed consent;
(b) measure magnetic stimulated quadriceps twitch (QuadTw) strength bilaterally;
(c) randomize patients to treatment with either:
Sham therapy, consisting of bilateral placement of All-Stim 2 electrodes for 30 minutes a day without activation of the electrical circuitry of the unit, or
Active therapy, using the All-Stim 2 electrodes to actively produce a rhythmic quadriceps contraction for 30 minutes a day.
We plan to have a total of 24 patients in the study, with two patients randomized to active treatment for every one patient given sham treatment. As a result we anticipate the final group studied will include 14-16 active treatment patients and 6-8 sham treatment patients.
(d) continue these regimens daily for 7 days;
(e) remeasure magnetic stimulated QuadTw on day 8;
(f) the research team will visit the patient until discharge and will record duration of mechanical ventilation, duration of ICU stay, and total duration of hospitalization; and,
(g) patients will be visited by a member of the research team at 28 days after study entry to assess the distance that can be walked in 6 minutes (i.e. the 6 minute walk test) and to assess patient well being using the St. Georges
Research Questionnaire (SGRQ, a commonly used and extensively validated instrument to assess patient well being).
We also review each patient's chart on acceptance into the study to obtain demographic information including the following: age, sex, diagnoses, medications, reason for institution of mechanical ventilation, vital signs at the time of the initial visit, bedside parameters of mechanical ventilation use (including mode of ventilation, duration of ventilation, level of oxygen, breath volume and rate, % triggered breaths), most recent arterial blood gas values, and chest radiograph readings at the time of the initial visit.

Attachments

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Study Population: Describe the characteristics of the subject population, such as anticipated number, age range, gender, ethnic background and health status. Identify the criteria for inclusion and exclusion. Explain the rationale for the use of special classes such as fetuses, pregnant women, children, institutionalized, adults with impaired consent capacity, prisoners, economically or educationally disadvantaged persons or others who are likely to be vulnerable.

If women or minorities are included, please address how the inclusion of women and members of minority groups and their subpopulations will help you meet your scientific objectives. Exclusion of women or minorities requires clear and compelling rationale that shows inclusion is inappropriate with respect to the health of the subjects or that inclusion is inappropriate for the purpose of the study. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be excluded routinely from participation in clinical research.

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;
- The proposed dates of enrollment (beginning and end);
- The proposed sample composition of subjects.

You may reference grant application/sponsor's relevant protocol pages and attach as an appendix using the below attachment button, however, a summary paragraph must be provided in the text box below.

Inclusion into the study will be considered for all adult patients requiring mechanical ventilation for more than 48 hours for respiratory failure in one of the University of Kentucky adult ICU's. We will include patients regardless of gender, race, or adult age. It is hoped that sufficient minorities and women will be studied so that the subject population is representative of the general patient population, but we will be somewhat constrained by the numbers of available patients and the day to day makeup of the patient population in the UK ICU's. Inclusion of minorities and women will make the study results more generally applicable.
Patients will be excluded:
(a) if the physician caring for the patient determines that the patient is too unstable to tolerate these measurements,
(b) if the patient requires high dose pressors (more than 15 mcg/min of norepinephrine or more than 15 mg/kg/min of dopamine),
(c) if the patient requires more than 80% FiO2 or more than 15 cm H2O of PEEP,
(d) if the patient has a cardiac pacemaker or implanted defibrillator,
(e) if the patient has received neuromuscular blocking agents within the 48 hours preceding testing,
(f) if the patient has a history of a preexisting neuromuscular disease,
(h) if the patient has profound and uncorrectable hypokalemia (less than 2.5) or hypophosphatemia (less than 1.0)
(i) if the patient is a pregnant female,
(j) if the patient is a prisoner,
(k) if the patient is institutionalized,
(l) if it is thought that the patient is terminal and will have care withdrawn within 7 days.

Our goal is to recruit 24 total patients into the study. We plan to study an additional 12 patients over the next 12 month period (1 patient/month).

Attachments

Subject Recruitment Methods & Privacy: Using active voice, describe plans for the identification and recruitment of subjects, including how the population will be identified, and how initial contact will be made with potential subjects by those having legitimate access to the subjects' identity and the subjects' information.

Describe the setting in which an individual will be interacting with an investigator or how and where members of the research team will meet potential participants. If applicable, describe proposed outreach programs for recruiting women, minorities, or disparate populations as participants in clinical research. Describe steps taken to minimize undue influence in recruiting potential participants.

Please note: Based upon both legal and ethical concerns, the UK IRB does not approve finder's fees or "cold call" procedures made by research staff unknown to the potential participant. The ORI/IRB does not control permission to any UK listserv, mass mailing list, etc. Investigators must secure prior approval for access and use from owners/managers.

For additional details, see topic "Recruitment of Subjects/Advertising" on ORI's IRB Survival Handbook web page and the PI Guide to Identification and Recruitment of Human Subjects for Research [PDF].

The PI and/or Dr. Callahan will meet 3-5 times a week with the MICU attendings at the University of Kentucky to identify patients who would be suitable candidates for this study based on the study inclusion and exclusion criteria. The MICU attending will then approach the patient and the patient's family to determine if the patient agrees to allow the PI and/or Dr. Callahan to discuss the study with them. The PI and/or Dr. Callahan will then approach the family and review the study with them.

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Advertising: Specify if any advertising will be performed. If yes, please see "IRB Application Instructions - Advertisements" for instructions on attaching copies of the information to be used in flyers or advertisements. Advertisements must be reviewed and approved by the IRB prior to use. For additional details, see topic "Recruitment of Subjects/Advertising" on ORI's IRB Survival Handbook web page for the *PI Guide to Identification and Recruitment of Human Subjects for Research* [D7.0000] document [PDF]. If you will be recruiting subjects via advertising at non-UK owned or operated sites, you should include a copy of written permission from that site to place the advertisement in their facilities.

Note: Print and media advertisements that will be presented to the public also require review by UK Public Relations (PR) to ensure compliance with UK graphic standards, and equal opportunity language. See Advertising Instructions for PR contacts.

No advertising will be performed.

Attachments

Informed Consent Process: Using active voice, describe the consent/assent procedures to be followed, the circumstances under which consent will be sought and obtained, the timing of obtaining informed consent, whether there is any waiting period between informing the prospective subject and obtaining consent, who will seek consent., steps taken to minimize the possibility of coercion or undue influence, the method used for documenting consent, and if applicable who is authorized to provide permission or consent on behalf of the subject. Note: all individuals authorized to obtain informed consent should be designated as such in the E-IRB "Study Personnel" section of this application.

Describe provisions for obtaining consent/assent among any relevant special populations such as children (see Children in Research Policy [PDF] for guidance), prisoners (see Summary of Prisoner Regulations [PDF] for guidance), and persons with impaired decisional capacity (see Impaired Consent Capacity Policy [PDF] for guidance). Describe, if applicable, use of specific instruments or techniques to assess and confirm potential subjects' understanding of the nature of the elements of informed consent and/or a description of other written materials that will be provided to participants or legally authorized representatives. If you have a script, please prepare it using the informed consent template as a guide, and submit it on a separate page.

Informed Consent for Research Involving Emancipated Individuals
If you plan to enroll some or all prospective subjects as emancipated, consult with UK legal counsel **when preparing the IRB application and prior to submitting the application to the IRB**. Include legal counsel's recommendations (legal counsel's recommendations may be attached in the E-IRB "Additional Information" section as a separate document, if necessary). For a complete definition of emancipated minors, see the section on *Emancipated Individuals* in the Informed Consent SOP [PDF].

Informed Consent for Research Involving Non-English Speaking Subjects
If you are recruiting non-English speaking subjects, the method by which consent is obtained should be in language in which the subject is proficient. Describe the process for obtaining informed consent from prospective subjects in their respective language (or the legally authorized representative's respective language). In order to ensure that individuals are appropriately informed about the study when English is their second-language, describe a plan for evaluating the level of English comprehension, and the threshold for providing a translation, or explain why an evaluation would not be necessary. For additional 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 [PDF]

After reviewing the study with the patient and their family, the PI and/or Dr. Callahan will ask the patient and the family if they wish to participate. The consent form will be reviewed with the patient and their family detailing the risks associated with the planned measurements. If the patient and family agree, the consent form will be signed. If the patient and their family wish they can think about the study and the PI will return the next day. After the consent form is signed, QuadTw measurements will be performed the same day and All-Stim 2 therapy will be started. The PI (Dr. Gerald Supinski) or Dr. Callahan will obtain all informed consents for the study. To eliminate coercion, all families and study recipients will be told that refusal to participate will in no way influence their care while at the University of Kentucky. Consent will be documented by having both the patient and the next of kin sign the consent form. Because most ICU patients receive some form of sedation, it is the intent of the PI to always inform the family as well as the patient and always have the family member with decision making power over the patient's care (e.g. their spouse or family member with power of attorney) sign the consent form. We will always seek to have the patients also sign the consent form. Under certain circumstances the patient may be so disabled that signage of the consent form is not possible (e.g. the patient is sedated or both hands are instrumented with IV's and pressure transducers). In the event of mental or physical inability of the patient to sign the consent form, the next of kin alone will sign the form.

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Research Procedures: Describe the research procedures that will be followed. Identify all procedures that will be carried out with each group of subjects. Differentiate between procedures that involve standard/routine clinical care and those that will be performed specifically for this research project.

It will first be verified that the patient does not meet any exclusion criteria and that informed consent has been obtained.

Quadriceps Twitch: For this assessment, we will place a quadriceps board (Bailey Manufacturing) under the leg, positioned so that the knee lies immediately over the apex of the apparatus. We will then strap a force transducer (Interface, Model SSM-AJ) over the lower leg, positioned at one-fourth the distance between the lateral malleolus of the ankle and the knee. We will first assess twitch force with the apparatus set at the fourth "peg" position, corresponding to a 90o angle between the thigh and lower leg (we have found this corresponds to the optimal angle for quadriceps force generation in the majority of subjects). We will then adjust magnetic field strength during femoral nerve stimulation to ensure optimization of twitch force (i.e. usually at 85% of the maximum Magstim magnetic field strength). Five consecutive twitches will be performed at this setting. Subsequently, to verify the 90o knee angulation setting represents the optimal preload, twitches will be repeated at knee angle settings above and below 90o (i.e. at "peg" settings of 2 and 6). The average of the three best twitch forces generated at the optimal knee angle with supramaximal field strength will be averaged and this measure will be reported as the quadriceps twitch force.The technique will be repeated using the other leg. These measurements should take approximately 20 minutes.

All Stim 2: This device consists of a central controller which is attached to four soft adhesive electrodes. Two adhesive electrodes are placed over the quadriceps on each leg (two electrodes on the right, two electrodes on the left for a total of four electrodes). Once these electrodes are positioned, the controller is turned on and a stimulation regimen is selected. We will use a program in

which 45 Hz frequency current is used, with an on duration of 1 second and an off duration of 3 seconds; current intensity will be increased until the force generated by the quadriceps is 60% of the force generated by the quadriceps in response to magnetic twitch stimulation during the prior preliminary strength testing. (We have performed preliminary tests in normal individuals indicating that this level of force activation is well tolerated and produces a demonstrable reproducible submaximal quadriceps contraction). Once this current intensity is identified, all subsequent training trials will use this level of current density for training studies. Sham training will be performed with a setting of zero current intensity. Stimulation will be carried out as a single session per day with each session lasting 30 minutes.

Initial Clinical Parameters: These parameters will be obtained from the medical record using values collected as closely as possible to the time at which initial QuadTw physiological data measurements are made. Parameters will include age, sex, diagnoses, medications, reason for institution of mechanical ventilation, vital signs at the time of the initial visit, bedside parameters of mechanical ventilation use (including mode of ventilation, duration of ventilation, level of oxygen, breath volume and rate, % triggered breaths), most recent arterial blood gas values, and chest radiograph readings. To provide an assessment of pre-hospital function, family members will be asked four questions: (a) how far could the patient ambulate, (b) how many flights of steps could the patient go up, (c) which activities of daily living (dressing, carrying objects, performing daily grooming tasks), if any, were impaired, and (d) did the patient have difficulty standing from a sitting position or lifting objects over their head.

Hospital Outcomes: After recruitment into studies, electronic hospital records will be reviewed twice a week to determine the time from the point of initial study measurements to successful weaning from mechanical ventilation (defined as remaining off all mechanical ventilation for more than 4 days). Alternative outcomes that will be recorded, for patients that are not weaned from mechanical ventilation, include transfer to a chronic facility for long term weaning from mechanical ventilation (i.e. an LTAC) or death. Deaths will be further subclassified as death due to withdrawal of care and death due to progression of disease. We will also record total ICU stay, total days of hospital stay, and incidence of recurrent respiratory failure, defined as a requirement for reintubation either during the initial hospitalization or at any time out to day 28 after entry into the study. We will also record hospital readmission rates.

Follow-up Visit (28 days). At follow-up visits we will assess the distance walked in 6 minutes and we will ask patients if they have returned to work (either full time or part time). We will also have patients fill out the St. Georges respiratory questionnaire (SGRQ) on return visits. This questionnaire evaluates patient's perceptions about their respiratory health, including their assessment of the ability to perform simple tasks of daily living. The PI and/or Dr. Callahan will visit the patient's domicile (or other site of habitation) to obtain these assessments.

Attachments

Data Collection: List the data or attach a list of the data to be collected about or from each subject (e.g. interview script, survey tool, data collection form for existing data).

If the research includes survey or interview procedures, the questionnaire, interview questions or assessment scales should be included in the application (use attachment button below).

The data collection instrument(s) can be submitted with your application in draft form with the understanding that the final copy will be submitted to the IRB for approval prior to use (submit final version to the IRB for review as a modification request if initial IRB approval was issued while the data collection instrument was in draft form).

Note: The IRB approval process does not include a statistical review. Investigators are strongly encouraged to develop data management and analysis plans in consult with a statistician.

See above section which includes all this information.

Attachments

Resources: Describe what resources/facilities are available to perform the research (i.e., staff, space, equipment). Such resources may include a) staffing and personnel, in terms of availability, number, expertise, and experience; b) psychological, social, or medical services, including counseling or social support services that may be required because of research participation; c) psychological, social, or medical monitoring, ancillary care, equipment needed to protect subjects; d) resources for subject communication, such as language translation services, and e) computer or other technological resources, mobile or otherwise, required or created during the conduct of the research. Please note: Some mobile apps may be considered mobile medical devices under FDA regulations (see FDA Guidance). Proximity or availability of other resources should also be taken into consideration, for example, the proximity of an emergency facility for care of subject injury, or availability of psychological support after participation.

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); supportive documentation can be attached in the E-IRB "Additional Information" section. Provide a written description of the role of the non-UK site(s) or non-UK personnel who will be participating in your research. The other site may need to complete its own IRB review, or a cooperative review arrangement may need to be established. Contact the Office of Research Integrity at (859) 257-9428 if you have questions about the participation of non-UK sites/personnel.

If the University of Kentucky is the lead site in a multi-site study, or the UK investigator is the lead investigator, describe the plan for managing the reporting of unanticipated problems, noncompliance and submission of protocol modifications and interim results from

the non-UK sites.

The PI has studied various aspects of respiratory muscle function and dysfunction over a 25 year period. During this time, the PI has published approximately 100 peer reviewed papers on original research related to respiratory muscle and other critical care topics, as well as 150 abstract presentations at national meetings.
The PI is currently funded by an NIH grant as PI and also receives support as a co-investigator from another NIH grant held by Dr. Callahan. The PI's laboratory is equipped with a cart containing all the apparati required to obtain QuadTw measurements. Specifically, the cart is equipped with two MagStim 200 magnetic stimulators equipped with dual figure of eight coils for nerve stimulation, the quad board used for positioning the leg, and a force transducer with a computer interface. This cart is mobile and can be moved to the ICU rooms when needed to assess leg strength. The cart is equipped with sterile wipes that will be used to disinfect all exposed surfaces before and after entrance and exit from patient rooms. Both the Magstim and
All Stim 2 units are FDA approved and are in common usage in the USA and other countries for assessment of neurological function and quadriceps conditioning, respectively.

Potential Risks: Describe any potential risks or likely adverse effects of the drugs, biologics, devices or procedures subjects may encounter while in the study. Please describe any physical, psychological, social, legal or other risks and assess their likelihood and seriousness.

Use of magnetic twitch stimulation for femoral nerve stimulation is essentially painless. Use of the All-Stim 2 device produces a mild tingling sensation but is also essentially painless at the settings we will use. Removal of the All-Stim 2 electrodes, which have sticky adhesives on their inner surface, could theoretically cause pain in a very hairy individual (this will be dealt with as described below). Both devices could theoretically produce problems in individuals with pacemakers or implanted defibrillators, so patients with these devices will be excluded from the study. We will ask patients to perform a six minute walk test at 28 days after discharge and use a pedometer to assess distance walked. This test has been previously used to assess patient outcomes after ICU discharge (see references 1, 2) with no reported complications. There is essentially no risk to performance of chart reviews or evaluation using the SGRQ.

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Safety Precautions: Describe the procedures for protecting against or minimizing any potential risks, *including risks of breach of confidentiality or invasion of privacy*. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse events, or unanticipated problems involving subjects. Also, where appropriate, describe the provisions for monitoring the data collected to ensure the safety of subjects. If vulnerable populations other than adults with impaired consent capacity are to be recruited, describe additional safeguards for protecting the subjects' rights and welfare.

Extremely unstable patients, i.e. patients requiring high levels of PEEP, high levels of oxygen or in severe shock, will be excluded from study.

There are no reported adverse effects using magnetic stimulation to assess peripheral nerves except for an isolated report of interference with pacemaker function in one patient. For this reason, we will exclude patients with pacemakers from this study.

There is no risk to the patient for chart review assessment.

There have no reports of previous injury with use of the All Stim 2 device. Application of the All Stim 2 device will require placement of sticky pads on the anterior thighs so, as a result, removal of the device could cause some pain if the sticky pads pull on the thighs of an excessively hairy individual. For this reason, if a patient has significant thigh hair we will warn them of this risk and offer to remove the thigh hair (i.e. by shaving or use of Nair) prior to use of the device. Both the PI and Dr. Callahan have used the device without incident; we would not expect the average patient to be so hairy that this should represent a serious concern.

Benefit vs. Risk: Describe potential benefits to the subject(s); include potential benefits to society and/or general knowledge to be gained. Describe why the risks to subjects are reasonable in relation to the anticipated benefit(s) to subjects and in relation to the importance of the knowledge that may reasonably be expected to result. If you are using vulnerable subjects (e.g., impaired consent capacity, pregnant women, etc…), justify their inclusion by describing the potential benefits of the research in comparison to the subjects' vulnerability and the risks to them. For information about inclusion of certain vulnerable populations, see the IRB/ORI Standard Operating Procedure for Protection of Vulnerable Subjects [C3.0100] [PDF].

The sensation associated with magnetic stimulation is not painful but is associated with a sudden involuntary contraction of the muscles being stimulated distal to the nerve. The use of the All Stim 2 device produces a tingling sensation.

We do not believe these techniques pose a significant risk to patients, in that no long term adverse consequences should occur providing the exclusion criteria used for this study are rigorously followed.

There are, however, important potential benefits for the patients taking part in this study. Use of this rehabilitation technique may well increase leg strength, improve ambulation, facilitate early mobilization, shorten ICU and hospital stays, improve long term mobility, and increase the long term ability of patients to perform activities of daily living.

Available Alternative Treatment(s): Describe alternative treatments and procedures that might be advantageous to the subjects, should they choose not to participate in the study. This should include a discussion of the current standard of care treatment(s).

Currently these patients receive only minimal levels of passive range of motion in the ICU to try to maintain leg muscle function. There

is no alternative exercise regimen that is currently being employed routinely in the MICU at the University of Kentucky.

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Research Materials, Records and Privacy: Identify the sources of research material obtained from living human subjects. Indicate what information (specimens, records, data, genetic information, etc.) will be recorded and whether use will be made of existing specimens, records or data. Explain why this information is needed to conduct the study.

Return of Research Results or Incidental Findings (if applicable):
If research has the potential to identify individual results or discover incidental findings that could affect the health of a subject, describe plans to assess, manage, and if applicable disclose findings with individual subjects or provide justification for not disclosing. For IRB expectations, refer to the UK IRB “Frequently Asked Questions (FAQs) on the Return of Research Results or Incidental Research Findings" [PDF].

All data collected from the study (i.e. tracings of force measurements, demographic/clinical data obtained from chart review,) will be placed in a folder which will be stored in a locked filing cabinet in the office of the principal investigator in MN616. None of this information will be shared with other investigators. All folders will be given a study number and further analysis of mean data obtained from patient study folders will be carried out with only the patient study number as identification. Folders containing mean data will also be stored in the locked filing cabinet in MN616.

Confidentiality: Specify where the data and/or specimens will be stored and how the researcher will ensure the privacy and confidentiality of both. Please address the following items or indicate if the following has been addressed in a HIPAA or Limited Review form:

- physical security measures (e.g., locked facility, limited access);
- data security (e.g., password-protection, data encryption);
- who will have access to the data/specimens and identifiers;
- safeguards to protect identifiable research information (e.g., coding, links, certificate of confidentiality);
- procedures employed when sharing material or data, (e.g., honest broker if applicable, written agreement with recipient not to re-identify, measures to ensure that subject identifiers are not shared with recipients).
- management after the study

Describe whether data/specimens will be maintained indefinitely or destroyed. If maintained, specify whether identifiers will be removed from the maintained information/material. If identifiers will not be removed, provide justification for retaining them. If the data/specimens will be destroyed, describe how and when the data/specimens will be destroyed. For multi-site studies, the PI consults the study sponsor regarding retention requirements, but must maintain records for a minimum of six years after study closure. Also, specify who will access the identified data/specimens, and why they need access. If applicable, 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 entities not affiliated with UK.

HIPAA/FERPA Minimal Access Standards: The IRB expects researchers to access the minimal amount of identifiers to conduct the study and comply with applicable HIPAA and Family Educational Rights and Privacy Act (FERPA) requirements. If data are going to be collected, transmitted, and/or stored electronically, for appropriate procedures please refer to the guidance document "Confidentiality and Data Security Guidelines for Electronic Data" [PDF].

Cloud storage: For storage of data on cloud services other than UK OneDrive, please verify security settings are sufficient and in accordance with respective departmental, UK Corporate Compliance, and/or UK Information Technology requirements.

Creation of digital data application/program: If a research protocol involves the creation and/or use of a computer program or application, mobile or otherwise, please specify whether the program/application is being developed by a commercial software developer or the research team and provide any relevant information regarding the security and encryption standards used, how data is stored and/or transmitted to the research team, what information about the subjects the program/application will collect, etc. For relevant information to include, see Considerations for Protocol Design Concerning Digital Data [PDF]. The IRB may require software programs created or used for research purposes be examined by a consultant with appropriate Internet technology expertise to ensure subject privacy and data are appropriately protected.

NIH-funded genomic research: The National Institutes of Health (NIH) Genomic Data Sharing (GDS) Policy sets forth expectations that ensure the broad and responsible sharing of genomic research data consistent with the informed consent of study participants from which the data was obtained. If you are submitting genomic data to an NIH data repository, describe your NIH data sharing plan.

Management after study: Describe how the collected data/specimens will be managed after the end of the study. Specify whether identifiers will be removed from the maintained information/material. If identifiers will not be removed, provide justification for retaining them and specify what steps will be taken to secure the data/specimens (e.g., maintaining a coded list of identifiers separate from the data/specimens).

If the data/specimens will be destroyed, describe how, when, and why this will be done. Note that destruction of primary data may violate NIH and NSF retention and sharing requirements, journal publication guidance, and University Data-Retention policies. Additionally, primary data may be necessary for other purposes (to validate reproducibility, for data sharing, or for

evidence in various investigations). PIs should carefully consider whether the destruction of data is justified.

The investigator is responsible for retaining signed consent and assent documents and IRB research records for at least six years after study closure, as outlined in the Study Closure SOP [PDF]. If the research falls under the authority of the FDA or other regulatory agencies, or a study sponsor is involved, additional requirements may apply.

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For publication, no individual identifying features of the patients will be included in abstracts and papers generated using the data collected in this study. As indicated in section 13, all records will be kept in a locked file cabinet in the PI's office. The records for this study will be kept until seven years after the data is published, in keeping with current NIH recommendations on data archiving. The data will be kept in the locked file cabinet in MN616 at least until the data is published and then transferred to a second locked archival filing cabinet in the PI's office. At seven years after publication all data will be destroyed by shredding the documents.

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Payment: Describe the incentives (e.g., inducements) being offered to subjects for their time during participation in the research study. If monetary compensation is offered, indicate how much the subjects will be paid and describe the terms and schedule of payment. (It is IRB policy that provision should be made for providing partial payment to subjects who withdraw before the completion of the research. Monetary payments should be prorated or paid in full.)

No subject will be paid for participation in the study

Costs to Subjects: Describe any costs for care associated with research (including a breakdown of standard of care procedures versus research procedures), costs of test drugs or devices, and research procedure costs that are the subject's responsibility as a consequence of participating in the research. Describe any offer for reimbursement of costs by the sponsor for research related injury care.

There will be no cost to subjects for participation 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, clinical research, or NIH-funded/FDA-regulated clinical investigations.

If you are conducting greater than minimal risk research, clinical research, or your clinical investigation is NIH-funded/FDA-regulated, 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, clinical research, or your clinical investigation is FDA-regulated, *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.

If relying on an independent agent or committee for DSMB services, it is the PI's responsibility to establish the services with the agent or committee. Please be reminded that the PI must submit DSMB reports to the IRB via modification or continuing review.

To monitor the long term conduct of the study, including monitoring of adverse effects, we will employ a study monitoring board consisting of Dr. David Mannino and Dr. James McCormick. Dr. Mannino is a well recognized epidemiologist with a background in statistics and his expertise will be used to make the appropriate statistical analysis of the data obtained from these studies. Dr. McCormick is the Division Chief of Pulmonary/Critical Care Medicine who has had experience in physician compliance with ICU procedures and monitoring of patient safety in the conduct of invasive ICU procedures and he will have responsibility for assessment of safety issues. This board will review the study at twelve month intervals. At these meetings the board will evaluate the quality of the collected data, completeness of data collected for each patient studied, will review the eligibility form to assess compliance with inclusion/exclusion criteria, reporting of adverse effects by patients or nurses, will determine if the study should be continued or terminated because of safety/risk issues, and, at the final meeting, will review the final results.

Adverse effects will be recorded on study forms and reviewed by the DSMB. The DSMB will consider stopping the study if they conclude that excessive adverse effects clearly linked to one of the treatment arms are occurring. The board will compile a report for each meeting and present their findings to the PI.

To date there have been no adverse events..

No studies have been conducted in the last year so no DSMB assessment of the study has been performed since the last submission of this protocol. We will submit data to the DSMB once new subjects have been recruited.

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Subject Complaints: Describe procedures (other than information provided in consent document) for handling subject complaints or requests for information about the research. The procedures should offer a safe, confidential, and reliable channel for current, prospective, or past research subjects (or their designated representative) permitting them to discuss problems, concerns and

questions, or obtain information.

After obtaining consent, the patient and his family will be given a sheet providing the office number, paging number, and cell phone for the PI and instructions on how to contact the PI. We will provide the patient and his family any information obtained from the QuadTw measurements, and will provide them with information as to whether the measured numbers are normal or reduced. If any complaints are registered by a subject these will be recorded and placed in the patient's study file. This information will be handled in a confidential matter (see above).

Does your research involve **Non-English Speaking Subjects or Subjects from a Foreign Culture**?

○ Yes ◉ No

Non-English Speaking Subjects or Subjects from a Foreign Culture

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.

Include contact information for someone who can act as a cultural consultant for your study. The 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 have any direct involvement with the study. If you do not know someone who would be willing to act as your cultural consultant, the Office of Research Integrity will try to find someone to fill this role (this may delay the approval process for your protocol). Please include the name, address, telephone number, and email of the person who will act as the cultural consultant for your study. For more details, see the IRB Application Instructions on Research Involving Non-English Speaking Subjects or Subjects from a Foreign Culture.

For recruitment of Non-English speaking subjects, the consent document needs to be in the subject's native language. Download the informed consent template available in the E-IRB "Informed Consent/Assent Process" section and use it as a guide for developing the consent document. (Note: Your translated consent document can be attached to your application in the "Informed Consent" section; **be sure to save your responses in this section first**.)

If research is to be conducted at an international location, identify local regulations, laws, or ethics review requirements for human subject protection. If the project has been or will be reviewed by a local Ethics Committee, attach a copy of the review to the UK IRB using the attachment button below. You may also consult the current edition of the International Compilation of Human Research Standards

Does your study involve **HIV/AIDS research and/or screening for other reportable diseases (e.g., Hepatitis C, etc…)**?

○ Yes ◉ No

HIV/AIDS Research

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

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

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

PI-Sponsored FDA-Regulated Research

Is this an investigator-initiated study that:

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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 PI 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 your (the PI's) experience/knowledge/training (if any) in serving as a sponsor (e.g., previously held an IND/IDE); and
- Indicate if you have transferred any sponsor obligations 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 PI completed the mandatory PI-sponsor training prior to this submission?

○ Yes ○ No

If you (the PI) have completed equivalent sponsor-investigator training, you may 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

Attach Type	File Name
Authorization	10650-Form-J_HIPAA_Authorization_revised .doc

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:

Note: Inpatient studies are required by Hospital Policy to utilize the Investigational Drug Service (IDS). 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" [PDF].

Please also complete and attach the Study Drug Form (PDF) (required):

Attachments

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:

All Stim Electrical Stimulator

Is the study being conducted under a valid Investigational Device Exemption (IDE) or Humanitarian Device Exemption (HDE) application? See UK HUD SOP (PDF) for guidance.

○ Yes ◉ No

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

IDE/HDE Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

Other: ☐ Held By:

☐ Check if this is a Treatment or Compassionate Use IDE under the Food and Drug Administration (FDA) Early 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 Clinical Investigations, Compassionate Use, and Treatment IDE SOP" [PDF]

Does the intended use of any device used 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.

Please also complete and attach the Study Device Form (PDF) (required):

Attachments

Attach Type	File Name
StudyDevice	Study Device Attachment(for PDF) All Stim.pdf
StudyDevice	FDAAllstim.pdf
StudyDevice	K024036.pdf

RESEARCH SITES

0 unresolved comment(s)

In order for this section to be considered complete, you must click "SAVE" after ensuring all responses are accurate.

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

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

*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.

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**, you must describe the plan for the management of reporting unanticipated problems, noncompliance, and submission of protocol modifications and interim results from the non-UK sites in the E-IRB "Research Description" section under *Resources*.

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, such as the establishment of a cooperative IRB review agreement with the non-UK site. Questions about the participation of non-UK sites/personnel should be discussed with the ORI staff at (859) 257-9428.

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
☐ Aging Research
☐ Alcohol Abuse Research
☐ Cancer Research
☐ Certificate of Confidentiality
☐ CCTS-Center for Clinical & Translational Science
☐ Clinical Research
☑ Clinical Trial
☐ Clinical Trial Multicenter(excluding NIH Cooperative Groups)
☐ Clinical Trial NIH cooperative groups (i.e., SWOG, RTOG)
☐ Clinical Trial Placebo Controlled Trial
☐ Clinical Trial UK Only
☐ Collection of Biological Specimens
☐ Collection of Biological Specimens for Banking
☐ Community-Based Participatory Research
☐ Data & Safety Monitoring Board
☑ Data & Safety Monitoring Plan
☐ Deception
☐ Drug/Substance Abuse Research
☐ Educational/Student Records (e.g., GPA, test scores)
☐ Emergency Use (Single Patient)
☐ Genetic Research
☐ Gene Transfer
☐ GWAS (Genome-Wide Association Study) or NIH-funded study generating large scale genomic data
☐ International Research
☐ Internet Research
☐ Planned Emergency Research Involving Waiver of Informed Consent
☐ Pluripotent Stem Cell Research
☐ Recombinant DNA
☐ Survey Research
☐ Transplants
☐ Use of radioactive material, ionizing radiation, or x-rays [Radiation Safety Committee review required]
☐ Vaccine Trials

Click applicable listing(s) for additional requirements and/or 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 (look up "What is the definition of....)

  Determine if research meets NIH definition of clinical trial;
  *Reminder: Ensure compliance with applicable requirements including:
  - Clinicaltrials.gov registration;
  - Good Clinical Practice (GCP) training; and
  - Consent Posting Requirement [PDF] for federal funded trials.

- 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 of radioactive material, ionizing radiation or x-rays for research

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/or 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 [PDF]
- DoJ) Department of Justice or Bureau of Prisons ([PDF]
- (DoE) Department of Energy Summary [PDF] and Department of Energy Identifiable Information Compliance Checklist [PDF]
- (EPA) Environmental Protection Agency [PDF]

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.):

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 DoD resources. (See DoD SOP [PDF] and DoD Summary [PDF] 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)

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/or upload form [WORD] [PDF]
- Radioactive Drug Research Committee (RDRC)--information
- Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)**--Attach MCC PRMC materials, if any, per instructions
- See requirement of Office of Medical Education (OME)
- See requirement of Graduate Medical Education Committee (GME)

Attachments

**** If you are proposing a study involving cancer research, be sure to have "Cancer Research" marked in the E-IRB "Research Attributes" section.** If your study involves cancer research, ORI will provide a copy of 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 PRC 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 (e.g., serial #):

Submission Description: If you wish to have specific details included in your approval letter (e.g., serial #, internal tracking identifier, etc…), type in the box below exactly what you wish to see on the approval letter. What you type will automatically appear at the top of all approval letters, identical to how you typed it, until it is changed by you (Hint: don't include instructions or questions to ORI staff as those will appear in your approval letter). **If these details need to be changed as a result of revisions, continuation review, or modifications to the application, you are responsible for updating the content of the field below accordingly.**

Protocol/Product Attachments - For each item checked, please attach the corresponding material.

- ☐ Detailed protocol
- ☐ Dept. of Health & Human Services (DHHS) approved protocol (such as NIH sponsored Cooperative Group Clinical Trial)
- ☐ Drug Documentation (e.g., Investigator Brochure; approved labeling; publication; FDA correspondence, etc.)
- ☐ Device Documentation (e.g., Manufacturer information; patient information packet; approved labeling; FDA correspondence, etc.)
- ☑ Other Documents

Protocol/Product Attachments

Attach Type	File Name
AddInfoProduct	Protocol Form B All Stim 2 2017 (2).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.

Additional Materials:

If you have other materials you would like to include in your application for the IRB's consideration, please attach using the Attachments button below.

[To view what materials are currently attached to your application, go to "Application Links" in the menu bar on the left and click "All Attachments".]

Attachments

SIGNATURES (ASSURANCES)

0 unresolved comment(s)

On all IRB applications there is a requirement for additional assurances by a Department Chairperson (or equivalent) [hereafter referred to as "Department Authorization" (DA)], and when applicable, a Faculty Advisor (FA) (or equivalent), which signifies the acceptance of certain responsibilities and that the science is meritorious and deserving of conduct in humans. Note: the individual assigned as DA *should not* also be listed in the Study Personnel section, the individual assigned as FA *should* be listed in the Study Personnel section.

For a list of responsibilities reflected by signing the Assurance Statement, download the guidance document "What does the Department Chairperson's Assurance Statement on the IRB application mean? [PDF]"

Required Signatures:

First Name	Last Name	Role	Department	Date Signed	
David	Moliterno	Department Authorization	Internal Medicine	04/24/2018 02:52 PM	View/Sign
Gerald	Supinski	Principal Investigator	Internal Medicine	04/24/2018 01:37 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 will not be able to be sent to the Office of Research Integrity/IRB.

Please remember to update, when applicable, the Approval Letter Details text box under the Additional Information section to ensure verbiage you want on your approval letter is accurate.

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 a message will be forthcoming 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.

	Document Type	File Loaded	Document Description	File Size	Modified By	Mod Date
	ApprovalLetter	ApprovalLetter.pdf		0.080	jato226	2/17/2021 4:15:22 PM
	Stamped Consent Form	Consent Form All Stim 2 for 2017.pdf		0.163	jato226	2/17/2021 4:15:22 PM
	Stamped Consent Form	Consent Form All Stim 2 for 2017.pdf		0.163	jato226	2/17/2021 4:15:22 PM
	Assent	Consent Form All Stim 2 for 2017.pdf	Informed Consent	0.160	gsupi2	2/26/2019 10:16:36 AM
	AddInfoProduct	Protocol Form B All Stim 2 2017 (2).pdf		0.108	gsupi2	4/24/2018 1:34:21 PM
	StudyDevice	K024036.pdf	Device Information (Second)	0.454	gsupi2	4/24/2018 1:30:41 PM
	StudyDevice	FDAAllstim.pdf	Device Information	0.984	gsupi2	4/24/2018 1:30:00 PM
	StudyDevice	Study Device Attachment(for PDF) All Stim.pdf	Device Form	0.745	gsupi2	4/24/2018 1:29:36 PM
	Authorization	10650-Form-J_HIPAA_Authorization_revised .doc		0.038	gsupi2	4/24/2018 1:17:06 PM
	Informed ConsentParental Permission	Consent Form All Stim 2 for 2017.pdf		0.160	gsupi2	4/24/2018 12:54:14 PM
	ImpairedConsent	Form_T_2Cii.doc		0.089	gsupi2	4/24/2018 12:48:39 PM

Protocol Changes

Protocol Number: 44530

No Changes

There are no recorded changes tracked for this protocol.

Study Personnel Changes:

No Changes

There are no recorded changes to study personnel.

No comments