Document Coversheet

Study Title: Utilization of Nebulized Heparin for Patients Receiving Mechanical Ventilation for COVID19-associated Acute Respiratory Failure

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	01/31/22
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Coversheet created:	09/20/22

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.

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 ***

COVID19 Utilization of Nebulized Heparin for Patients Receiving Mechanical Ventilation for COVID19-associated Acute Respiratory Failure

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.

COVID19 Nebulized Heparin

Anticipated Ending Date of Research Project: 2/10/2024

Number of human subjects (or records/specimens reviewed): 46

Study is/will be open to new subject enrollment or data/specimen collection: (•) 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 to 80

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

Enter Numbers Only!

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

If unknown, please explain why: Limited to the demographics of the population treated within the University of Kentucky Medical Intensive Care Unit

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)

- ☐ Children (individuals under age 18)
- ☐ Wards of the State (Children)
- ☐ Emancipated Minors
- ☐ Students
- ☐ College of Medicine Students

ADDITIONAL INFORMATION:

Please visit the IRB Survival Handbook under the named topic:

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

- ☐ 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

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.pdf

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
Informed ConsentHIPAA Combined Form	Informed Consent RedCap.pdf
Informed ConsentHIPAA Combined Form	Informed Consent 03.24 Clean.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.

The electronic medical record will be utilized to determine patient eligibility. No component of this aspect of the study is greater than minimal risk. While this is a prospective study to placebo versus nebulized heparin, informed consent will be obtained prior to enrollment.

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

To protect the confidentiality of the patient, data will be housed in a password-protected master list spreadsheet. Once data has been collected, this sheet, linking the medical record number and unique study number will no longer be used. Data will be analyzed and reported in a de-identified form.

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

The investigators require the use of the electronic medical record in the pre-screening period to identify patients on the basis of the current admission and diagnosis and therapy received. For this, we will need access to the patient chart to guarantee study eligibility. Without this access, the study could not be completed. The filter within the electronic medical record will only pull patients who meet inclusion criteria. The chart will then be utilized to verify this information and exclude patients who meet the exclusion criteria.

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

After identifying that a patient is eligible for the study, they or their LAR will be approached with the attached informed consent and provided with pertinent information for the study. If they decline further participation, the electronic medical record will not be accessed by the investigators following.

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

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

Identifiable patient information (the medical record number) is needed to track the patient throughout the duration of the study - this will allow the investigators to data collect the information provided above as well as the location of the patient for blood draws. The patient identifiable information will be kept separate from both the biospecimens and the data collection form on RedCap. Instead, a master list, tying the identifiable patient information to a designated subject, onidentifiable code will be kept by the PI only on the PI's laptop. The non-identifiable assigned code will be placed on the biospecimens and into RedCap to tie subject data to their biospecimen.

☐ 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.

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.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel coronavirus, emerging first in December 2019. Since then, over eight million patients have tested positive for coronavirus disease 2019 (COVID-19), with a hospitalization count exceeding 63,000 patients. (1) Over 40% of hospitalized patients with COVID-19 develop acute respiratory distress syndrome (ARDS), with mortality exceeding 60%. (2) The optimal therapeutic approach to COVID-19 ARDS remains unknown, with multiple failed trials of agents targeting SARS-CoV-2 and the resulting inflammatory response. (3-6) To date, the focus of COVID-19 supportive care research has focused on the immune response incited by this novel coronavirus; however, recent data show that the cytokine response elicited within COVID-19 is minimal relative to other ARDS populations. (7) Rather, COVID-19 ARDS appears to have a higher incidence of coagulopathy compared to historic ARDS populations. (7) Namely, COVID-19 ARDS is associated with altered plasma coagulation markers, such as increased D-dimer, increased prothrombin time, and a lower platelet count compared to alternative ARDS causes. (8-12) Pulmonary microvascular clot formation is a known feature of COVID-19 ARDS; however, such clots are commonly not identified until such clots propagate to larger, clinically detrimental venous thromboembolic events (VTE). (8-12) Microvascular thrombosis worsens pulmonary function through several mechanisms and correlates with illness severity, respiratory failure, and mortality in ARDS. (13)

COVID-19 coagulopathy has a significant impact on patient outcomes. (14) The incidence of VTE has been reported to exceed 30% in some studies. (15) Several guidelines have made recommendations regarding therapeutic systemic anticoagulation to prevent or treat VTE in COVID-19, with the majority recommending therapeutic anticoagulation only once a thromboembolic event is found or highly suspected. (16) More aggressive strategies of systemic anticoagulation for VTE prevention pose a high risk of bleeding and thus are not currently recommended. (16) While the thrombotic mechanisms in COVID-19 patients are not clear, they may involve both increased coagulation and decreased fibrinolysis. Standard anticoagulation, such as heparin, inhibits activation of coagulation, promotes anticoagulant tissue factor pathway inhibitor expression, reduces procoagulant tissue factor expression, and increases endothelial expression of heparin sulfate.

Nebulized heparin has a potential benefit in contrast to systemic heparin, given its direct effects on the pulmonary vasculature. Because of its route of administration, higher doses are seen locally, increasing efficacy within the respiratory tract and reducing the risk of system bleeding. (13) Systemic absorption is minimal, allowing for much higher doses of heparin to be administered via inhalation compared to standard systemic doses. (17) Further, nebulized heparin has the potential to inhibit pulmonary viral replication. In previous trials of nebulized heparin for the treatment of non-COVID-19 ARDS, nebulized heparin was shown to decrease alveolar dead space fraction and tidal volumes, while also increasing days free of mechanical ventilation. (18-19) Early nebulized heparin has the potential to decrease clot formation directly at the site of onset, preventing VTE events and later the need for systemic anticoagulation while improving overall oxygenation. In a recent randomized controlled study of 256 patients with ARDS, nebulized heparin was not associated with an increase in adverse events (5% of 128 patients in the heparin group vs 2% of 124 patients in the placebo group; OR 2·33 [0·59 to 9·24]; p=0·23). (20)

Preliminary data suggest that coagulopathy is highly prevalent and potentially perpetuates COVID-19 ARDS and VTE. In our preliminary work at the University of Kentucky, we evaluated coagulation profiles in patients with COVID-19 (in-patients and outpatients) compared to control. Patients with COVID-19 had decreased plasma anticoagulant protein S. Additionally, patients with COVID-19 had more procoagulant plasma when compared to controls, and systemic anticoagulation did not appear to influence these factors. Currently, systemic anticoagulation is provided only once a known thromboembolic event occurs. We hope to prevent this resistant prothrombotic phase with the use of early inhaled heparin in contrast to systemic administration after known VTE. The objective of the current study is to investigate the utilization of nebulized heparin to circumvent this pathologic change and prevent harmful effects possible with systemic anticoagulation.

1. Coronavirus-19. CDC. Accessed October 27, 2020 from: https://gis.cdc.gov/grasp/covidnet/COVID19_5.html.
2. Wu C, Chen X, Cai Y, et al. Y. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020;180(7): 934–43.

3. Guaraldi G, Meschiari M, Cozzi-Lepri A, et al. Tocilizumab in patients with severe COVID-19: a retrospective cohort study. Lancet Rheumatol. 2020;2(8):e474-e484..
4. Stone JH, Frigault MJ, Serling-Boyd NJ, et al. Efficacy of Tocilizumab in Patients Hospitalized with Covid-19. N Engl J Med. 2020 Oct 21.
5. Grein J, Ohmagari N, Shin D, et al. N Engl J Med. 2020;382(24):2327-2336.
6. Liu STH, Lin HM, Baine I, et al. Convalescent plasma treatment of severe COVID-19: a propensity score-matched control study. Nat Med. 2020 Sep 15.
7. Leisman DE, Ronner L, Pinotti R, et al. Cytokine elevation in severe and critical COVID-19: a rapid systematic review, meta-analysis, and comparison with other inflammatory syndromes. Lancet Respir Med. 2020;16:S2213-2600(20)30404-5.
8. Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. Clinical Infectious Diseases. 2020;ciaa248.
9. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan. China Lancet. 2020;395(10223):497–506.
10. Deng Y, Liu W, Liu K, et al. Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 (COVID-19) in Wuhan, China: a retrospective study. Chin Med J. 2020;133(11):1261–7.
11. Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. J Thromb Haemost. 2020;18:1094–9.
12. Helms J, Tacquard C, Severac F, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med. 2020;46:1089–98.
13. van Haren FMP, Page C, et al. Nebulised heparin as a treatment for COVID-19: scientific rationale and a call for randomised evidence. Crit Care. 2020 Jul 22;24(1):454. doi: 10.1186/s13054-020-03148-2.
14. Nadkarni GN, Lala A, Bagiella E, et al. Anticoagulation, Bleeding, Mortality, and Pathology in Hospitalized Patients With COVID-19. J Am Coll Cardiol. 2020;76(16):1815-1826. doi: 10.1016/j.jacc.2020.08.041.
15. Hadid T, Kafri Z, Al-Katib A. Coagulation and anticoagulation in COVID-19. Blood Rev. 2020:100761.
16. Flaczyk A, Rosovsky RP, Reed CT, Bankhead-Kendall BK, Bittner EA, Chang MG. Comparison of published guidelines for management of coagulopathy and thrombosis in critically ill patients with COVID 19: implications for clinical practice and future investigations. Crit Care. 2020;24(1):559.
17. Dixon B, Santamaria JD, Campbell DJ. A phase 1 trial of nebulised heparin in acute lung injury. Crit Care. 2008;12(3):R64.
18. Dixon B, Schultz MJ, Smith R, Fink JB, Santamaria JD, Campbell DJ. Nebulized heparin is associated with fewer days of mechanical ventilation in critically ill patients: a randomized controlled trial. Crit Care. 2010;14(5):R180.
19. Dixon B, Smith R, Santamaria JD, et al. A trial of nebulised heparin to limit lung injury following cardiac surgery. Anaesth Intensive Care. 2016;44(1):28–33.
20. Dixon B, Smith RJ, Campbell DJ, Moran JL, Doig GS, Rechnitzer T, MacIsaac CM, Simpson N, van Haren FMP, Ghosh AN, Gupta S, Broadfield EJC, Crozier TME, French C, Santamaria JD; CHARLI Study Group. Nebulised heparin for patients with or at risk of acute respiratory distress syndrome: a multicentre, randomised, double-blind, placebo-controlled phase 3 trial. Lancet Respir Med. 2021 Jan 22:S2213-2600(20)30470-7. doi: 10.1016/S2213-2600(20)30470-7. Epub ahead of print. PMID: 33493448; PMCID: PMC7826120.
21. National Heart, Lung, and Blood Institute PETAL Clinical Trials Network, Moss M, Huang DT, et al. Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome. N Engl J Med. 2019;380(21):1997-2008. PMC6741345.
22. Haudebourg AF, Perier F, Tuffet S, et al Respiratory Mechanics of COVID-19- versus Non-COVID-19-associated Acute Respiratory Distress Syndrome. Am J Respir Crit Care Med. 2020;202(2):287-290.

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 primary objective of this study is to evaluate the efficacy of nebulized heparin administration in COVID-19. Our primary outcome will be defined as the mean PaO2/FiO2 ratio in the first 10 days of ICU stay. This is the gold standard for hypoxia monitoring in ARDS. Our secondary safety outcome will include clinically significant bleeding, defined as transfusion of red blood cells, required intervention for new-onset bleeding, or death attributed to bleeding during the study period. Additional outcomes will include incidence of VTE, time on mechanical ventilation, ICU duration, and overall mortality.

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]

We propose a randomized, controlled pilot study of patients admitted with confirmed COVID-19 receiving mechanical ventilation for ARDS (paO2/FiO2 ratio =300) within 48 hours. Enrollment will occur by the ICU research team who perform daily review for study enrollment. Patients will be randomized to nebulized heparin (25,000 units in 3 mL sodium chloride [NaCl] every 6 hours) versus

placebo (5 mL nebulized NaCl every 6 hours) for 10 days or until successful ventilator wean. Drugs will be dispensed by investigational drug services. Patients will be excluded for a history of heparin allergy, terminal status as determined by attending physician, history of thrombosis (prior VTE or cardiovascular event), high risk of bleeding (platelet count < 50,000/μL or international normalized ratio > 1.5), or active bleeding. Monitoring will include daily ventilator parameters, complete metabolic panels, and complete blood counts, as well as hourly vital signs as part of standard care. The MICU also has an actively enrolling biobank with respiratory samples which we will use to assess viral load. Additional samples will be collected for coagulation (protein S, thrombin, and histone) monitoring, at baseline, 72 hours, and day 10. Laboratory results, medication administration, and vital sign data will be collected up until 10 days of ICU admission or discharge. Mortality, length of stay, and mechanical ventilation duration will be collected for the entire hospital stay. Based on expected baseline paO2/FiO2 ratio of 118 mmHg, we calculate that we need a sample size of 46 patients (n=23 per group) to detect a 15% improvement in paO2/FiO2 ratio, assuming an alpha of 0.05 and power of 80%. (22)

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.

Patients admitted with confirmed COVID-19 receiving mechanical ventilation for ARDS (paO2/FiO2 ratio =300) will be included.

Patients will be excluded for the following:
- Allergy to heparin
- Any history of heparin-induced thrombocytopenia
- High risk of bleeding (platelet count < 50,000/μL or international normalized ratio > 1.5)
- Patients with known bleeding disorders (i.e. hemophilia or von Willebrand Disease)
- Active bleeding
- Pulmonary bleeding during this hospital admission (Pulmonary bleeding is frank bleeding in the lungs, trachea or bronchi with repeated hemoptysis, or requiring repeated suctioning, and temporally associated with acute deterioration in respiratory status)
- Neurosurgical procedures during this hospital admission or such procedures are planned
- Epidural catheter in place
- Any history of intracranial, spinal or epidural hemorrhage
- Tracheostomy in place
- Cervical spinal cord injury associated with reduced long-term ability to breathe independently
- Spinal or peripheral nerve disease with a likely prolonged reduction in the ability to breathe independently
- Receiving extra-corporeal membrane oxygenation or cotinuous renal replacement therapy
- Usually treated with hemodialysis or peritoneal dialysis for end-stage renal failure
- Death is deemed imminent or inevitable or there is an underlying disease with a life expectancy of fewer than 90 days
- Pregnant or might be pregnant.
- Objection from the treating clinician
- Consent refused by the patient or substitute decision maker.
- History of thrombosis (VTE or cardiovascular event)

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].

Potential subjects will be screened based on a screening filter that the study team has previously used in the electronic medical record to screen for studies of acute respiratory failure. Once identified, a study team member will approach the patient's care team to inquire about the study. If allowed, the team member will assess the patient for ability to provide consent as described. If the patient is not eligible to provide informed consent, the legally authorized representative will be approached for written or electronic consent.

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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.

N/a

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]

Once subjects are identified per the above process, an assessment will be made as described in form T by the study team member of whether the patient can provide informed consent. If ineligible, a legally authorized representative will be approached regarding the study. Informed consent will be sought once the patient meets the eligibility criteria as defined in the study protocol. If the legally authorized representative is not physically in the hospital due to visiting restrictions due to COVID-19, an electronic consent process will be sought as follows. The patient's LAR will be contacted via telephone and approached about the study in the same way that the LAR would be if they were physically present. If the LAR is interested in pursuing further, a member of the study team will send the LAR a RedCap link that has been designed for e-consent in this study. A member of the study team will walk the LAR through the e-consent document, which mirrors the written informed consent document exactly, and answer any questions along the way. If the LAR consents, they will sign the document using the e-sign feature in RedCap. A member of the study team will email the LAR back with a copy of the signed e-consent 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.

Patients will be screened for eligibility by a member of the research team. If a patient meets eligibility, then a team member will approach the LAR for informed consent. After enrollment, the patient will be randomized via an online randomization generator to either nebulized heparin (25,000 units in 3 mL sodium chloride [NaCl] every 6 hours) or placebo (5 mL nebulized NaCl every 6 hours) for 10 days or until successful ventilator wean. The nurse will be approached for a 10 mL blood draw to be performed at baseline, 72 hours, and day 10 to assess protein S, thrombin, and histone in the Wood laboratory (BBSRB B306-15 and B306-16). The study team will collect the blood samples. Up to 10 mL of blood will be drawn each time for a maximum of 30 mL total, collected in citrate-containing tubes. Deidentified data will be collected via RedCap from the standard of care charting. Upon study completion, deidientified data will be sent to the statistician for analysis.

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.

The following will be reocrded from standard of care documentation: demographics (age, sex, race, past medical history), chief complaint, past medical history, blood gases, medications, and transfusions administered and dosing, mechanical ventilation parameters, complete blood counts, complete metabolic panels, and vital signs. Patient outcomes including in-hospital mortality, Murray Lung Injury Score, ICU and hospital length of stay, the incidence of venous thromboembolism, the incidence of pulmonary embolism, the incidence of clinically significant bleeding, and duration of mechanical ventilation. Lab values for coagulation (protein S, thrombin, and histone) monitoring with an additional blood draw at baseline, 72 hours, and day 10.

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.

Co-investigators as outlined in this IRB application. Research personnel to assist with recruitment and sample processing. Laboratory space from Dr. Wood's laboratory (BBSRB B306-15 and B306-16) and the CCTS Biomarker Analysis Laboratory.
For the Wood Laboratory:
Staff: Dr. Wood is an expert in the coagulation field and has been working in this field since 2004. Martha Sim, a graduate student in Dr. Wood's laboratory, will process blood samples, perform the in vitro experiments, and store leftover samples for future studies. Both Dr. Wood and Ms. Sim have completed CITI training for human subjects research and the responsible conduct of research.
Space: Dr. Wood's laboratory (B306, BBSRB) encompasses ~500 ft2 with benches and desks for 4 individuals. Student desk space is adjacent to the laboratory benches. The laboratory is in an "open" format, with other groups on either side of the Wood laboratory space.
Equipment: The centrifuge required for processing the blood samples and the locked freezer for sample storage are available in Dr. Wood's laboratory. Dr. Wood also has all of the equipment required for the experiments described in the research plan.
Computers: Computers are available to the study team in Dr. Wood's laboratory and office. These computers are part of the UK health center network and require UK login credentials. Once logged in, study team members will have access to the shared folder where study-related documents are stored. Anyone who is not a member of the study team will not have access to this folder. In addition, non-identifiable results will be stored in a LabArchives folder, to which study team members will have access.

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.

Risks associated with drawing blood from the intravenous line are minimal, but may include discomfort, bruising, soreness, infection, excess bleeding, clotting, light headedness, or fainting. Risks of nebulized heparin, although rare, include bleeding and an increase in partial prothrombin time.

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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.

Researchers will take steps to keep the information confidential. Researchers will not list identifiable information on samples stored in the laboratory, but use a key linked back to a master list maintained on a password-protected computer. The patients will be in the

intensive care unit and subject to the intensive monitoring required from the baseline care of such a population. Once the database has been completed from information collected, identifiable information will be removed and replaced with a subject ID number. The PI will maintain a logbook of the ID number with patient identifiers in a locked cabinet in a locked office. If clinically significant bleeding occurs during drug treatment, defined as transfusion of red blood cells thought to be secondary to investigational drug or required intervention for new-onset bleeding secondary to investigational drug, the drug will be automatically stopped.

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].

We do not know if subjects in this group will benefit directly, but hypothesized benefits of the use of nebulized heparin include decreased length of stay and decreased lung injury scores. Risks are outlined in the informed consent document and notably include the risk of bleeding. Given the mortality rate in patients with ARDS secondary to COVID-19, there may be patients that benefit from this drug despite the minimal risks. We have attempted to use the literature to guide our protocol to reflect those patients most likely to benefit.

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).

There are no alternative treatments. Patients enrolled will continue to receive standard of care therapies per the discretion of the primary team. Thromboprophylaxis is permitted per standard of care. Patients who require systemic anticoagulation will be excluded from this study.

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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].

Blood specimens will be obtained and processed as described above. This information will be used for research purposes only. The collection of these samples will be documented in the patients' medical records. Patients will be assigned a unique patient number that can only be linked to PHI by study personnel. This master list will be stored on the PI's password-encrypted laptop, located within a locked office. No physical documents will be utilized for this study. We maintain the right to keep, preserve, use, and dispose of the findings of this protocol in accordance with institutional guidelines. The appropriate offices of the federal government (e.g. OHRP) maintain the right to inspect the records of the study at any time. Investigational records from this study will be maintained in a confidential manner; subject names will not be associated with any published results. In the circumstance that a subject regains capacity to provide informed consent after samples have been collected and the subject declines participation in the study, samples will be discarded according to the UK Biological Safety Manual section 10.0 and UK Environmental Management will be contacted.

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 (If the research is non-sponsored you need a data use agreement to share data/specimens [Transfer Agreements]).

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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During and after this study, the participants' identities will be kept confidential to the extent permitted by law. Patients will be identified by a code, and, except as set forth below, personal information from subjects' records will not be released to any third party without written permission. Subjects will not be personally identified in any publication or presentation about this study. However, the records may be reviewed, under the guidelines of the Health Insurance Portability and Accountability Act (HIPAA), by the FDA, United States Department of Health and Human Services. Additionally, local site personnel, agents of the University of Kentucky, the Institutional Review Board may review the records including those with identifying information. The information may be disclosed if the recipients described above are not required by law to protect the privacy of the information.

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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.)

Patients will not receive any financial inducements for their participation in this 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.

Drug costs will be covered by the sponsor. All other costs associated with this study are considered standard of care. The patients' insurance company, Medicare or Medicaid will be responsible for the costs of all care and treatment that they receive during this study that they would normally receive for their condition. These are costs that are considered medically reasonable and necessary and will be part of the care the patient would receive if they did not take part in this study.

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

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

The PI and/or Co-Investigators will review all adverse events on a routine basis. The subjects are ICU patients and undergo continuous monitoring by the medical team during the blood draws performed as part of this study. The physicians that monitor the subjects are intensive care physicians trained to perform these tasks as part of routine care and manage these patients. The nurses are also present and continuously monitoring the patient during the procedure, providing additional expertise.

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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.

Contact information for the study coordinators and Principal Investigator will be provided to the subject should they desire additional information or wish to file a complaint about the study. Additionally, the patient's nurses and physicians will be able to contact the study team should the patient have any questions or concerns. The ORI's contact information will also be provided wish to have further information/discussion on their rights as a participant in research. All complaints or information requests shall be passed along the appropriate channels to provide answers or notify the appropriate individuals of a complaint.

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

○ Yes ◉ No

Non-English Speaking Subjects or Subjects from a Foreign Culture

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

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

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

Has the sponsor-investigator completed the mandatory PI-sponsor training prior to this submission?

○ Yes ○ No

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

Attachments

HIPAA

0 unresolved comment(s)

Is HIPAA applicable? ◉ Yes ○ No

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

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

☐ HIPAA De-identification Certification Form

☑ HIPAA Waiver of Authorization

Attachments

Attach Type	File Name
Waiver	Form K 03.24 Clean.pdf

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:

Unfractionated Heparin

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

Attach Type	File Name
StudyDrug	Form O.pdf

STUDY DEVICE INFORMATION

0 unresolved comment(s)

A DEVICE may be a:

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

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

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

○ Yes ◉ No

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

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

LIST EACH DEVICE BEING TESTED IN STUDY IN THE SPACE BELOW

Device Name:

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

○ Yes ○ No

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

IDE/HDE Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

Other: ☐ Held By:

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

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

- FDA expanded access approval or sponsor's authorization;
- An independent assessment from an uninvolved physician, if available;
- Confirmation of agreement from manufacturer or entity authorized to provide access to the product.

For guidance and reporting requirements at the conclusion of treatment see the "Medical Device Clinical Investigations, Compassionate Use, and Treatment IDE SOP" [PDF]

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

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

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

Attachments

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

Consent and Authorization to Participate in a Research Study

KEY INFORMATION FOR COVID19 Utilization of Nebulized Heparin for Patients Receiving Mechanical Ventilation for COVID19-associated Acute Respiratory Failure

We are asking you to choose whether or not to volunteer for a research study about the administration of heparin nebulization (inhalation) in patients admitted to the intensive care unit on a ventilator for COVID-19. We are asking you because you have been diagnosed with COVID-19 and have acute respiratory distress syndrome per your treatment team. This page is to give you key information to help you decide whether to participate. We have included detailed information after this page. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is below.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

By doing this study, we hope to learn whether heparin, a blood thinner, when given directly to your lungs, helps lung improvement when compared to placebo. Your participation in this research will last about 10 days. In order to do this, we will collect blood from you on 3 different days and we will monitor you until hospital discharge. More information on this procedure are provided later in this form.

The purpose of this research is to gather information on the safety and effectiveness of nebulized heparin. Heparin is approved by the Food and Drug Administration (FDA), but being tested for a different purpose.

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

If you are assigned to the placebo part of the study, you will not benefit directly, but will help to inform us and other healthcare professionals about the blood and how it clots in COVID-19 respiratory failure, a process which can be targeted for treatment.

If you are assigned to receive heparin, it could decrease the duration you require supplemental oxygen via the ventilator and may allow you to be discharged from the hospital sooner. For a complete description of potential benefits, refer to the Detailed Consent.

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

If you are assigned to receive heparin, this medication may carry a risk for bleeding and we highly recommend to your physician that you receive monitoring for such bleeding while in the ICU. About 3-5% of patients are reported to experience an adverse event, such as bleeding, while receiving this medication.

You might not want to volunteer for this study if you do not want your samples used for research. That is perfectly fine and declining to participate in this study will not affect your clinical care in any way. For a complete description of risks, refer to the Detailed Consent.

DO YOU HAVE TO TAKE PART IN THE STUDY?

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

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study contact Brittany Bissell, PharmD, PhD of the University of Kentucky, Department of Pulmonary, Critical Care, and Sleep and Pharmacy Practice and Science at

Phone: 740-541-3471

Email: brittany.bissell@uky.edu

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

DETAILED CONSENT:

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

If you are pregnant, have a heparin allergy, active bleeding, a history of bleeding, or an illness which requires a blood thinner to be administered within the vein, you do not qualify for this study.

WHERE WILL THE STUDY TAKE PLACE AND WHAT IS THE TOTAL AMOUNT OF TIME INVOLVED?

The research procedures will be conducted in the Medical Intensive Care Unit (MICU) at the UK Chandler Medical Center. All procedures will occur during hospital stay while you are in the MICU. Each visit will take about 10 minutes in total. The total amount of time you will be asked to volunteer for this study is up to 1 hour over the next 10 days.

WHAT WILL YOU BE ASKED TO DO?

- If you agree to participate, you will be asked to sign a consent form.
- Your treatment will not change based on enrollment in this study.
- Once the consent form is signed, we will collect one tube of blood – approximately 10 mL (2 tsp). This blood will be taken from a central line (a catheter in a large vein), if you have one, or a peripheral line, if not (a catheter within a smaller vein)
- Every effort will be made to collect blood at the same time as other standard of care blood draws. If no additional blood draws are ordered for the day, the sample will be collected at the same time of medication administration to decrease your interruptions throughout the day
- We will repeat this procedure at day three and day ten of your stay.
- You will receive either heparin or a control agent (sodium chloride) every 6 hours while on the mechanical ventilator, up to 10 days total.
- We will look at data from the medical chart during your stay in the hospital.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Loss of Confidentiality: Any time information is collected, there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Risks of Blood Draw: Risks associated with drawing blood from the intravenous line you already have are minimal, but may include discomfort, bruising, soreness, infection, excess bleeding, clotting, light headedness, or fainting. You will have up to 8 teaspoons of blood collected total as a part of this study.

Risks of Study Medication: In previous studies of nebulized heparin, there has been a 3-5% increase in risk of bleeding. This bleeding can be serious if it is in your lungs or brain. It is an uncommon risk and can be corrected either surgically or with blood products.

Possible Risk	How often has it occurred?	How serious is it?	Can it be corrected?
Bleeding anywhere other than lungs	It is extremely uncommon	Moderately serious	Yes; With blood products or surgery
Bleeding in lungs	It is extremely uncommon	Serious	Yes; With blood products or surgery
Heparin allergy	It is extremely uncommon	Very serious	Yes; With blood thinners
Changes in ventilator	It is extremely uncommon	Moderately serious	Yes; by changes from your lung doctor

There is always a chance that any medical treatment can harm you. The research treatments/procedures in this study are no different. In addition to risks described in this consent, you may experience a previously unknown risk or side effect.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

We do not know if you will get any benefit from taking part in this study. However, some people have experienced decreased time on the venitlator when receiving nebulized heparin during mechanical ventilation. If you receive placebo, you will not get any personal benefit from taking part of this study. However, if you take part in this study, information learned may help others with your condition.

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

If you do not want to be in the study, there are no other choices except not to take part in the study.

WHAT WILL IT COST YOU TO PARTICIPATE?

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

The University of Kentucky may not be allowed to bill your insurance company, Medicare, or Medicaid for the medical procedures done strictly for research.

Therefore, these costs will be paid by the study.

Your insurer, Medicare, or Medicaid, may agree to pay for the costs. However, a co-payment or deductible may be needed from you. The amount of this co-payment or deductible may be costly.

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

When we write about or share the results from the study, we will write about the combined information. 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. Any paper records will be kept in locked file cabinets in locked offices and you will be given a unique subject identifier number in our electronic databases that cannot identify you.

You should know that in some cases we may have to show your information to other people.

For example, the law may require or permit us to share your information with:

- a court or agencies, if you have a reportable disease/condition;
- authorities or a mental health professional if you pose a danger to yourself or someone else (e.g. suicidal thoughts).

To ensure the study Is conducted properly, officials of the Food and Drug Administration and the University of Kentucky may look at or copy pertinent portions of records that identify you.

REDCap is a secure, web-based program to capture and store data at the University of Kentucky. We will make every effort to safeguard your data in REDCap. However, given the nature of online surveys, we cannot guarantee the security of data obtained by way of the Internet.

CAN YOU CHOOSE TO WITHDRAW FROM THE STUDY EARLY?

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

If you choose to leave the study early, data collected until that point will remain in the study database and may not be removed.

The investigators conducting the study may need to remove you from the study. You may be removed from the study if:

- you are not able to follow the directions,
- we find that your participation in the study is more risk than benefit to you, or

- the agency paying for the study chooses to stop the study early for a number of scientific reasons.

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 discuss this with the investigator/your doctor before you agree to participate in another research study while you are in this study.

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

If you believe you are hurt or if you get sick because of something that is due to the study, you should contact your nurse and medical team immediately. Once they are informed, either you or they may contact Brittany Bissell, PharmD, PhD at 740-541-3471

Your medical team will determine what type of treatment, if any, is best for you at that time.

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

Medical costs related to your care and treatment because of study-related harm will be your responsibility.

A co-payment/deductible may be needed by your insurer or Medicare/Medicaid even if your insurer or Medicare/Medicaid has agreed to pay the costs. The amount of this co-payment/deductible may be costly.

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

We will tell you if we learn new information that could change your mind about staying in the study. We may ask you to sign a new consent form if the information is provided to you after you have joined the study.

WILL YOU BE GIVEN INDIVIDUAL RESULTS FROM THE RESEARCH TESTS?

Generally, tests done for research purposes are not meant to provide clinical information. We will not provide you with individual research results.

There is a slight possibility that during a research procedure, an investigator could discover something that could affect your health. If this occurs, it will be reviewed by the clinician investigator and, if necessary, discussed with your medical team. That information may be placed in your medical record and discussed with you. This will help in providing appropriate medical care.

WHAT ELSE DO YOU NEED TO KNOW?

If you volunteer to take part in this study, you will be one of about 50 people to do so.

The University of Kentucky is providing financial support and/or material for this study.

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

WILL YOUR INFORMATION (OR SPECIMEN SAMPLES) BE USED FOR FUTURE RESEARCH?

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

AUTHORIZATION TO USE OR DISCLOSE YOUR IDENTIFIABLE HEALTH INFORMATION

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

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

- All health information that is listed within the medical chart for this hospitalization (the hospitalization during which the study takes place) include but not limited to:
  - Demographics, including age, gender, and medical record number
  - Medical History and Physical Exam results related to this study
  - Laboratory test results
  - Vital signs
  - Medication data
  - Diagnostic images and findings related to this study
  - All diagnostic and medical procedures related to the study
  - Consultation reports and progress notes related to the study

The Researchers may use and share your health information with:

- The University of Kentucky's Institutional Review Board/Office of Research Integrity;
- Law enforcement agencies when required by law;
- University of Kentucky representatives;
- UK Hospital
- Investigational Drug Service (IDS)

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

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

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

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

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

- Send a written letter to: Brittany Bissell, PharmD, PhD inform her of your decision. Her address is: 740 South Limestone Street, KY Clinic J530, Lexington, KY 40536
- Researchers may use and release your health information **already** collected for this research study.
- Your protected health information may still be used and released should you have a bad reaction (adverse event).

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

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

INFORMED CONSENT SIGNATURES

This consent includes the following:

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

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

_____ **Signature of research subject** *or, if applicable, *research subject's legal representative*	_____ **Date**
_____ **Printed name of research subject**	
_____ **Printed name of research subject's legal representative*	
**If applicable, please explain Representative's relationship to subject and include a description of representative's authority to act on behalf of subject:* _____ _____	
_____ Printed name of [authorized] person obtaining informed consent and HIPAA authorization	_____ Date