Vanderbilt University Institutional Review Board

Application for Human Research
Health Sciences

SECTION 1:

1. Study Type Information

Indicate the category of minimal risk expedited review requested. From the categories presented below, check "**Yes**" for the categories that you believe describe your proposed research and "**No**" for all others. If none of the categories apply, complete an application for standard IRB review or contact the IRB staff for instructions.
Note: If you wish to request exemption status, submit ONLY the Request for Exemption.

YOU MUST CHECK "YES" OR "NO" FOR ALL OF THE FOLLOWING:

45 CFR 46.110(f)(1):
☐ Yes ☒ No **Clinical studies of drugs and medical devices only when condition (a) or (b) is met.**

(a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (NOTE: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
(b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

45 CFR 46.110(f)(2):
☐ Yes ☒ No **Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:**

(a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

(b) from other adults and children[2], considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

45 CFR 46.110(f)(3):
☐ Yes ☒ No **Prospective collection of biological specimens for research purposes by noninvasive means.**

Examples:
- hair and nail clippings in a nondisfiguring manner;
- deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
- permanent teeth if routine patient care indicates a need for extraction;
- excreta and external secretions (including sweat);
- uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;
- placenta removed at delivery;
- amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
- supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
- mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
- sputum collected after saline mist nebulization.

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45 CFR 46.110(f)(4):
☒ Yes ☐ No **Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.** Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

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

** This study wishes to collect data via a patient's physical exam, muscle strength testing, and questionnaires.**

45 CFR 46.110(f)(5):
☒ Yes ☐ No **Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).** ***NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects: 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.***

** This study wishes to collect data via a patient's standard of care shoulder radiographs, ultrasounds, and/or MRI, if taken as part of their clinical care.**

45 CFR 46.110(f)(6):
☐ Yes ☒ No **Collection of data from voice, video, digital, or image recordings made for research purposes.**

45 CFR 46.110(f)(7):
☐ Yes ☒ No **Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.** ***(NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects: 45 CFR 46.101(b)(2) except for children when the Investigators participate in the activities and (b)(3). This listing refers only to research that is not exempt.)***

SECTION 2:

2. Location of the Research

Is this proposal associated with any other IRB-approved studies?

☒ No
☐ Yes *If "Yes", please list IRB #(s):*

A. List all Performance Sites "engaged in research" *(insert additional rows if needed)*
An institution or performance site is "engaged in research" when its employees or agents (i) intervene or interact with living individuals for research purposes; (ii) obtain individually identifiable private information for research purposes; or (iii) if the institution receives a direct federal award to support such research. ***This may apply when a VU investigator collaborates with a non-VU investigator or institution, or when VU serves as a Coordinating Center. Please check all that apply and add additional sites. Each will require a letter of IRB approval. See IRB Policy*** *IRB Policy I.C.*

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Check all that apply	Name of Performance Site (list all participating sites below)	FWA Holding Institution	IRB of Record	IRB Approval
☒	Vanderbilt University (indicate where at VU): MCE, South Tower, Suite 3200	VUMC	☒ VU ☐ Other	☐ Attached ☒ Pending
☒	Vanderbilt Stallworth Rehabilitation Hospital	VUMC	☒ VU ☐ Other	☐ Attached ☒ Pending
☐	International Epidemiology Institute		☐ VU ☐ Other	☐ Attached ☐ Pending
☒	Other, specify: Brigham and Women's Hospital and Massachusetts General Hospital (Boston, MA)	Partners Healthcare FWA00008498	☐ VU ☒ Other	☒ Attached ☐ Pending
☐	Other, specify:		☐ VU ☐ Other	☐ Attached ☐ Pending
☐	Other, specify:		☐ VU ☐ Other	☐ Attached ☐ Pending
☐	Other, specify:		☐ VU ☐ Other	☐ Attached ☐ Pending

B. List all Performance Site(s) **not** engaged in research *(insert additional rows if needed)* ☒ **NA**
An institution or performance site is considered "not engaged in research" when its employees or agents **do not** (i) intervene or interact with living individuals for research purposes; or (ii) **does not** obtain individually identifiable private information for research purposes; or (iii) if the institution **does not** receive a direct federal award to support such research. **This applies if a VU investigator will be conducting research at a non-VU site or institution (e.g., when collecting specimens or information)**. Please refer to the instructions for examples of what may be considered "not engaged in research." *See IRB Policy I.C.*

Name of Performance Site	If the Performance Site has an IRB, a copy of the IRB approval letter is required.	If the Performance Site does ***not*** have an IRB, a letter of cooperation is required.
	☐ Attached ☐ Pending	☐ Attached ☐ Pending
	☐ Attached ☐ Pending	☐ Attached ☐ Pending

SECTION 3:
3. Funding Information

A. ☒ Internal Funding *(check all that apply)*:

☒ Departmental Funds ☐ No cost study ☐ Personal Funds
☐ Various Donors/Gifts ☐ Other, specify:

B. ☐ External Funding *(list all that apply; insert additional rows if needed)*:

Agency/Sponsor	Funding Mechanism
	☐ Grant ☐ Contract
	☐ Grant ☐ Contract

C. Is this study Industry-Supported? (If so, it is expected that the sponsor will pay the IRB new study fee of $2250 for initial review.)
☒ No ☐ Yes *If "Yes", please indicate method of payment below.*

For VU/VUMC:
☐ Please charge my account as follows:
Center Number: Account Number:

☐ Center and Account Number Pending—I will forward to the IRB when established.

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☐ Request for Waiver of IRB Fees attached—see application instructions.

For VSRH, IEI or other non-Vanderbilt sites, payment is required as specified in the signed MOU:

☐ I have attached a check payable to the "VU IRB" in the amount of $2250.

☐ Check requested – I will forward to the IRB when received

SECTION 4:

4. Purpose of the Study/Abstract.

Provide a brief abstract of the study in lay language. The IRB Committees are comprised of scientists with varied backgrounds, non-scientists, and community members.

Include the expected duration of the study.

Rotator cuff tears are one of the most common causes of shoulder pain. Evidence-based guidance on optimal diagnostic and treatment strategies for rotator cuff tears is lacking. Our proposed study aims to fill these gaps by identifying the prognostic factors which will predict better outcomes of rotator cuff tears of the shoulder, based on both operative and non-operative treatment. We will also compare outcomes of operative and non-operative treatment of rotator cuff tears and report on the best way to diagnose rotator cuff tears.

Subject data collection will occur over 10 years. The duration of the study is expected to last approximately 15 years.

5. Description of the Study.

A. Your description may include any or all of the following:

- background information;
- specific aims;
- hypothesis or research question;
- previous experience, including human and animal safety data, if applicable; and
- a critical evaluation of existing knowledge (relevant literature) about the research topic. A reference list and copies of pertinent articles can be appended if thought to be of value in the evaluation of the research by the IRB. ***Please contact the IRB if you need assistance in conducting a literature search.***

The IRB needs to understand how this study adds to the knowledge on this topic in order to be able to judge the risks and benefits to the research participants.

BACKGROUND AND SIGNIFICANCE

Rotator cuff tears account for 4.5 million physician visits and over one quarter million surgeries annually. They are a leading cause of shoulder pain and disability. Patients with rotator cuff tears present with shoulder pain and/or limitation in range of motion. Fourteen special physical exam tests have been described for diagnosis of rotator cuff tears. Prior literature describing sensitivity and specificity of these tests in diagnosing cuff tears is limited by retrospective design, small sample sizes, samples restricted to patients undergoing surgery, and failure to differentiate between partial and full thickness tears. As a result, there is little evidence to help clinicians interpret the diagnostic value of the clinical exam. Consequently, clinicians rely heavily on magnetic resonance imaging (MRI) for diagnosing cuff tears, adding considerable expense and delay in the diagnostic process.

The treatment options for rotator cuff tears are operative and non-operative. There is currently little consensus on indications and timing of rotator cuff surgery or non-operative treatment. A recent survey of 539 orthopedic surgeons showed significant variation in decision-making regarding whether a patient with cuff tear should receive surgery or non-operative treatment. Furthermore, there is lack of evidence-based guidance on factors associated with outcomes of operative versus non-operative treatment for cuff tears.

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A prospective study on comparison and predictors of good outcomes of rehabilitation and surgery would fill this void.

SPECIFIC AIMS

The proposal aims to recruit 600 participants into an observational longitudinal cohort study which will fill the evidence void in the assessment of diagnostic modalities (Aim 1) and identification of prognostic factors that predict better outcomes based on operative and non-operative treatment of rotator cuff tears (Aim 2). We propose to accomplish the following specific aims:

Aim 1: To determine sensitivity and specificity of symptoms and physical examination as compared with MRI and expert clinicians' diagnosis for the detection of rotator cuff tears.

Hypothesis 1a: Symptoms will be sensitive and nonspecific. Physical examination will have high sensitivity and low specificity in the detection of rotator cuff tears.

Hypothesis 1b: Combinations of select symptoms and physical examination findings will have greater sensitivity and specificity in diagnosing cuff tears than individual symptoms, physical examination findings, or imaging alone.

Aim 2: To prospectively assess outcomes of operative and non-operative treatments and predictors of pain relief and functional improvement following operative and non-operative treatment for rotator cuff tears.

Hypothesis 2a: Shorter symptom duration and smaller tear size predict greater pain relief and functional improvement following non-operative treatment.

Hypothesis 2b: Younger age, minimal tendon retraction, and absence of fatty infiltration predict greater pain relief and functional improvement following operative treatment as compared with non-operative treatment of rotator cuff tear.

Hypothesis 2c: In patients undergoing surgery, younger age, minimal tendon retraction, absence of fatty infiltration, partial thickness tear, better preoperative range of motion, and fewer comorbidities predict greater pain relief and functional improvement.

Aim 3: To determine inter-rater reliability of the diagnosis of rotator cuff tears.

Aim 4: To test inter- and intra-rater reliability of the diagnosis of rotator cuff tears and grading of muscle atrophy and fatty infiltration on imaging data.

Aim 5: To assess willingness of patients to participate in a hypothetical randomized controlled trial of operative versus non-operative treatment if they were offered one today.

STUDY PROGRESS TO DATE

This study already has an ongoing approved IRB protocol at Partners Healthcare in Boston and patient recruitment has been ongoing since 2011 at Brigham and Women's Hospital and Massachusetts General Hospital. The PI of the study in Boston is Nitin Jain, MD, MSPH. To date, approximately 375 patients with shoulder pain have been recruited. Of these, about 43% of patients have a rotator cuff tear and the remaining patients do not have a rotator cuff tear (but another reason for their shoulder pain such as arthritis, adhesive capsulitis). As of 5/13/2014, only patients with confirmed rotator cuff tears are being recruited at the Boston sites (detailed procedure outlined in Section 6).

We propose to start recruitment of only patients with confirmed rotator cuff tears at Vanderbilt using the IRB approved protocol at Partners Healthcare. Vanderbilt will become the coordinating site for the study once this protocol is approved and all patient follow-up (including patients already recruited at Partners Healthcare, patients who will be recruited in the future at Partners Healthcare, and patients recruited at Vanderbilt) will be conducted from Vanderbilt.

6. Minimizing Risks to Participants/Data and Safety Monitoring Plan (DSMP)

NOTE: If VU PI is accepting coordinating center responsibilities, address that specific role in each question below.

A. Describe how the risks to participants are minimized *(e.g., screening to assure appropriate selection of participants, identify standard of care procedures, sound research design, safety monitoring and reporting).*

Risks to participants will be minimized by implementing the following safeguards:

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- The PI and his co-investigators developed a study based on sound research design after performing an exhaustive literature search.
- Proper screening to ensure appropriate selection of patients, i.e. only patients fitting the study's inclusion criteria will be approached for participation in this study.

B. Describe how the risks to participants are reasonable in relation to anticipated benefits *(e.g., includes benefits to the individual as well as to human kind, indicate how the risks are justified in this population).*

We believe the risks of this study are minimal compared to the anticipated benefit, as no invasive (research-based) diagnostic testing will be performed. The risks associated with providing data for this research may be the release of the subject's name which could link them to the stored data and/or the results of the tests performed on these subjects. To minimize this risk, samples will be given a de-identified unique study code. Only designated research study staff will know the code. The name that belongs to the code will be kept in a locked file or in a computer with a password housed within the Departments of Orthopaedics and Physical Medicine and Rehabilitation, behind the Medical Center's firewalls. Only the study investigator and his study staff will have access to the link.

The risks associated with this study can be justified in this population since we hope that, in the future, other people might benefit from knowledge gained toward improving the understanding of the diagnosis and treatment of rotator cuff tears, treated both operatively and non-operatively.

C. Is there a data safety monitor or board/committee to review this study for safety and adherence to the study protocol? **NOTE: Regardless of the response to this question, all subsequent questions in this section must be addressed.**

☒ No
☐ Yes *If "Yes," describe the composition of the committee and their qualifications.*

D. Provide a general description of the data and safety monitoring plan.

According to NIH/NIAMS guidelines, this study (cohort design with no intervention) is not classified as a Phase I-IV clinical trial, and as such, no formal data safety and monitoring activities or board are required. Data for this study will be stored in locked file cabinets and only study staff will have access to it. Electronic data will be stored in password protected computers with only access to study staff.

E. Describe plans for monitoring the progress of trials and the safety of participants (e.g., timing of DSM reviews and reports, planned interim analysis, etc.). **Note: DSMB reports are required to be submitted to the IRB at the time of continuing review unless the information affects the risk/benefit profile of the study.**

We did not feel the need for a formal data safety monitor board because this is an observational cohort study. Progress of the study will be monitored by monthly data/enrollment reports. Safety of the participants will be monitored by the study coordinator and the PI on an ongoing basis.

F. Describe plans for assuring compliance with requirements regarding the reporting of adverse events (AEs), including plans for reporting of AEs to the IRB and appropriate regulatory agencies.

A designated research coordinator/analyst will be responsible for periodic data safety monitoring. They will be expected to report any adverse events to the IRB (as per policy and procedure). They will also report any adverse data safety events to the PI within 48 hours of their identification. The PI will review them within 72 hours and will notify the IRB Department within 7 business days.

G. Describe plans for assuring that any action resulting in a temporary or permanent suspension of a federally funded research project is reported to the grant program director responsible for the grant.

N/A

H. Describe plans for assuring data accuracy and protocol compliance.

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A designated research staff member at VUMC will be expected to report to the PI the number of eligible patients contacted during the previous quarter and how many of them consented or refused to participate in the study. The study coordinator will perform periodic quality assurance reviews to verify that the subjects they received informed consents for from VUMC are ones in which they can verify whether all data has been collected, and whether this data has been logged into the REDCap database.

7. ☐**Phase I** ☐**Phase II** ☐**Phase III** ☐**Phase IV** ☒**N/A (not a drug development trial) Please answer A-C if conducting a Phase I or II study.**

☐**Phase I/II** ☐**Phase II/III** ***(Note:*** *If more than one phase will be conducted under this application, then separate Informed Consent Documents are required.)*

A. Will participants have a baseline assessment for the status of the disease being studied?
(Baseline data should be collected/measured before the trial treatment commences. Baseline data may be collected from standard of care or research screening procedures. An example of baseline assessments may include: the collection of demographic and clinical characteristics of the trial participants; the collection of factors that are likely to modify any benefit of treatment, or those that may predict adverse reactions.)
☐ **No** ☐ **Yes**
Protocol reference:

B. Will participants have monitoring for the status of the disease being studied?
(Monitoring may be sequential, successive, or ongoing collection of data to evaluate, discover, or verify the clinical effect of interventions. The interventions may be done as standard of care or research procedures. Examples of monitoring may include imaging studies done for tumor measurements, collection of blood sampling for laboratory values, or data collected from quality of life questionnaires.)
☐ **No** ☐ **Yes**
Protocol reference:

C. Will there be discontinuation of research/study interventions with participants in the event of disease progression?
(For oncology studies this is defined as cancer that continues to grow or spread; however, for other diseases it may include the decline, deterioration, or degeneration of the participant or the worsening or aggravation of the condition under study.)
☐ **No** ☐ **Yes**
Protocol reference:

D. Therapeutic Intent (check one):

☐ The clinical trial has no therapeutic intent; it is designed to exclusively test toxicity or disease pathophysiology.

☐ The clinical trial has therapeutic intent* or the trial is testing diagnostic interventions and is enrolling healthy patient as a control group.
**A trial has therapeutic intent when the clinical trial protocol provides for the discovery, measurement, or verification of an effect of an investigational intervention on a participant with a diagnosed disease to determine whether the investigational intervention potentially improves the health outcomes for the participant. The trial must not be designed exclusively to test toxicity or disease pathophysiology. (Note: Studies involving only healthy volunteers would not qualify, as no improved health outcomes are expected for healthy volunteers.)*

If there is therapeutic intent in the clinical trial, please provide a brief narrative (and a reference to the section in the protocol) describing how the protocol design supports the above description of therapeutic intent for the individual participant:

☒ This is not a clinical trial (*An expanded definition is available in the application instructions*).

8. Is this a multicenter study in which Vanderbilt will serve as the coordinating center? (A multi-center study is one where different PIs at different institutions are conducting the same study).

☐ No *If "No," please skip to Item # 9*
☒ Yes *If "Yes," please complete the following:*

Has the Vanderbilt Coordinating Center PI assumed responsibility for any of the following:
A. Protocol and/or case report form development and/or distribution?
☐ No ☒ Yes

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B. Sample consent form development and/or distribution?
☐ No ☒ Yes
If "Yes," describe the coordinating center's role in reviewing modifications by the collaborating institution of sample consent information related to risks or alternative procedures to assure changes are appropriately justified (a copy of the sample consent form intended for distribution should be submitted with this application):

The PI at Vanderbilt will review modifications to consent forms at collaborating institutions to ensure that all changes are justified and risks and benefits are assessed. The consent form approved by the Partners IRB is attached with this application.

C. Critical documents (study) management?
☐ No ☒ Yes
For example, CC's may assume responsibility from the sponsor for tracking IRB approvals at each participating site, assuring IRB approval is granted prior to enrollment of participant at a participating center, and assuring no participants are enrolled prior to written IRB approval or during a lapse in approval (see the ICH guidelines section 8.2 for a listing of critical documents required before the trial commences and at the end of the trial and where the files are typically located).
If "Yes," describe the types of documents the coordinating center is responsible for managing:

The coordinating center is responsible for managing that IRB approval is obtained prior to enrollment of human subjects, for maintaining the Manual of Operating Procedures (MOOP) included in this submission, subject inclusion/exclusion, and tracking follow-up of subjects enrolled in the study. All study procedures and questionnaires are included with this application.

D. Site selection and training in study procedures?
☐ No ☒ Yes
If "Yes," briefly describe site selection, qualifications, site training and how training will be provided. *Please include how sites are selected (e.g., PI and key study personnel qualifications, experience, adequate resources and facilities).*

The Partners site for this study in Boston is already active and has recruited approximately 375 subjects in a Partners IRB approved protocol to date (approval attached). The Boston sites will continue to enroll subjects and Vanderbilt will be the coordinating center moving forward and also a site for recruitment. Site PI's have expertise in musculoskeletal research and have undergone human subjects research ethics and compliance trainings. Study personnel are also trained in the study protocol and have undergone ethics training. Study personnel and PI have access to password protected computers.

E. Assuring informed consent is obtained from each participant enrolled at the participating centers?
☐ No ☒ Yes ☐ N/A
If "Yes," describe the mechanisms to be employed, if "N/A," explain who is responsible for assuring informed consent is obtained:

Informed consent from each participant will be scanned/mailed to the coordinating site (Vanderbilt).

F. Tracking of serious adverse events and unanticipated problems involving risk to participants or others, reporting to participating centers and regulatory reporting?
☐ No ☒ Yes

G. Describe who will be responsible for receiving and reviewing serious adverse events and unanticipated problems involving risk to participants or others reported by the participating centers and how those reports will be disseminated to other participating centers, the coordinating center and participating site IRBs, sponsors, data safety monitoring boards and applicable regulatory agencies:

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Serious adverse events will be received and reviewed by the individual site PI's and by the PI at the Vanderbilt coordinating site. A designated research coordinator/analyst will be responsible for periodic data safety monitoring. They will be expected to report any adverse events to the IRB (as per policy and procedure). They will also report any adverse data safety events to the site and coordinating PI within 48 hours of their identification. The PI's will review them within 72 hours and will notify the IRB Department at the site and the coordinating center within 7 business days.

H. Will the coordinating center receive/store private, identifiable information about study participants from the participating centers?
☐ No ☒ Yes
If "Yes," specify the types of private, identifiable information, describe how it will be stored and for how long.

The Vanderbilt coordinating site will be responsible for conducting follow-up surveys, mailings, and phone calls of all participants in the study. The Boston sites have already recruited approximately 375 subjects and future follow-up of all of these subjects will be conducted from Vanderbilt once approved by the Vanderbilt IRB. Additionally, subjects who are recruited at the Boston sites in the future will also be contacted from Vanderbilt for mailings and phone calls, as Vanderbilt will serve as the coordinating center. Subjects will also be mailed their checks for completion of questionnaires from Vanderbilt.

All data including private identifiable data is stored as a hard copy in locked file cabinets and in a REDCap database at Partners that is HIPAA compliant. A copy of all study questionnaires, including private identifiable information, will be scanned/mailed to Vanderbilt using secure email or courier service. PI and staff at Vanderbilt will also have access to the REDCap database which contains all of this information. This information is needed to ensure that follow-up of subjects can be conducted from Vanderbilt and subjects can be paid for their participation in the study.

The private identifiable data includes names, medical record number, date of birth, social security number (for subject payment purposes), address, email address, and phone number. Data will be stored for the duration of the study in locked file cabinets and REDCap at Vanderbilt and only study staff will have access to this data.

I. Will coordinating activities include responsibilities that require contact with participants from the participating centers?
☐ No ☒ Yes
If "Yes," describe the reason for the contact, when and how the contact will be made; describe who will obtain consent, where consent will be obtained and how the coordinating center will assure consent was granted by the participant.

The Vanderbilt coordinating site will be responsible for conducting follow-up surveys, mailings, and phone calls of all participants in the study. The Boston sites have already recruited approximately 375 subjects and future follow-up of all of these subjects will be conducted from Vanderbilt once approved by the Vanderbilt IRB. Additionally, subjects who are recruited at the Boston sites in the future will also be contacted from Vanderbilt which will serve as the coordinating center. Subjects will also be mailed their checks for completion of questionnaires from Vanderbilt.

The consent will be obtained by a trained research assistant at each site and the coordinating center will receive a copy of the consent to assure that consent was granted by the participant.

J. Statistical Analysis
☐ No ☒ Yes
If "Yes," describe who will perform the statistical analysis and the qualifications of the individual performing the statistical analysis. In addition, describe whether the analysis will involve identifiable samples/information.

Statistical analysis will be performed by a data analyst with graduate level training in biostatistics at Vanderbilt. The data analyst will work under the guidance of a senior statistician at Vanderbilt and the PI. Statistical analysis will not be performed on identifiable data.

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K. Publication or Presentation of Study Results
☐ No ☒ Yes

L. Other Coordinating Responsibilities Not Already Described:
There are no additional coordinating responsibilities that were not previously described.

SECTION 5:

9. Subject Population(s)

Identify all categories or groups, primary or secondary target, age range, total number to be solicited, total number to be consented, and the number expected to complete the study. Primary targets are those who either give consent or those who can only provide assent (e.g., minors). Secondary targets are those who provide data to supplement the primary target data (e.g., parents completing a questionnaire, teachers who supply information and data).

Category/Group (e.g., adults, controls, parents, children, teachers, etc.)	**Primary or Secondary Target**	**Age Range** (e.g., 7-12, 13-17, adults)	**Number Directly Solicited** (applies only to mailed survey studies)	**Number to be Consented** (including withdrawals or screen failures)	**Number Expected to Complete the Study**
Adults with suspected rotator cuff tears	☒ Primary ☐ Secondary	≥ 45 yrs	225 ☐ N/A	225	191 (85%)
	☐ Primary ☐ Secondary		☐ N/A		
	☐ Primary ☐ Secondary		☐ N/A		
	☐ Primary ☐ Secondary		☐ N/A		

Insert additional rows if needed.

TOTALS from columns 4, 5, & 6	**225** ☐ **N/A**	**225**	**191**

10. Total number of participants stated in the protocol to be studied at all sites (regardless of PI).

N=600. This total of 600 subjects includes the approximately 375 subjects that have already been recruited at Brigham and Women's Hospital and Massachusetts General Hospital in Boston with a Partners Healthcare IRB approved protocol. Hence, approximately 225 additional subjects will be recruited in the future at Vanderbilt.

11. Does this study target one gender or specific social/ethnic group(s)?

☒ No
☐ Yes *If "Yes", please provide a rationale.*

12. Is the population being enrolled in this study at high risk for incarceration?

☒ No
☐ Yes *If "Yes," will the participants be withdrawn from the study once they are incarcerated?*
☐ Yes
☐ No *If "No," describe how re-contacting/re-consenting, treatment, and/or follow-up will occur.*

A. Check all that apply (*Complete and attach the appropriate supplemental form(s): ☒ NA

☐ Children/minors* (Form #1117) ☐ Pregnant women/fetal tissue/placenta* (Form #1116)

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☐ Cognitively impaired* (Form #1118) ☐ Prisoners* (Form #1115)

13. Does this study include any radiation ionizing procedure(s) for research?

☒ No
☐ Yes *If "Yes", please list:*

Note: Also, attach the appropriate HSRC/RDRC document(s).

SECTION 6:

14. Participant Identification, Inclusion/Exclusion Criteria, and Recruitment

A. Describe the specific steps to be used to identify and/or contact prospective participants. (If applicable, also describe how you have access to lists of potential participants. Scripts and advertisements should be submitted with this application or examples should be provided for any telephone contacts, advertisements, oral contact, etc.)

The Research Coordinator/Research Assistant (RA) will screen clinic patients scheduled to see a study physician within Vanderbilt University Medical Center. The screening will include browsing the reason for the patient's visit in the electronic scheduling system (Starpanel/Epic). All new patients presenting with shoulder pain will be shortlisted as potential recruits and cross- checked with the study's inclusion/exclusion criteria.

The Coordinator/RA will then review records of these shortlisted patients in Starpanel/Epic to include patients who meet the following criteria:

- ≥ 45 years of age and have an atraumatic rotator cuff tear
- Shoulder pain and/ or loss of range of motion for 4 weeks or more
- No history of prior shoulder fracture on the same side
- No history of prior shoulder surgery on same side
- No history of neck pain radiating to the shoulder or arm or hand

Enrollment Log: The Coordinator/RA will keep an Enrollment Log of all new patients presenting with shoulder pain that are potential recruits for the study. The enrollment log has information on demographics, reason for exclusion and whether the patient was recruited.

Eligibility Determination in Clinic:

The Coordinator/RA will make a list of all new patients presenting with shoulder pain who are 45 years or older from Starpanel prior to start of clinic. Once the potentially eligible patient has been seen by the attending physician who confirms the diagnosis of rotator cuff tear based on their clinical assessment and the patient has a MRI that documents a rotator cuff tear, the RA/coordinator will approach the patient for possible recruitment in the study.

The Coordinator/RA will fill out the screening form (with the help of the patient) which lists the inclusion and exclusion criteria. If all questions are answered "No", the Coordinator/RA will offer to provide information about the study and use the script in the document "RA Initial Recruitment Script_2_Only RCT_Vanderbilt"" (see attached).

If the patient consents to the study, the Coordinator/RA signs the Informed Consent form and also has the patient sign the Informed Consent Form. Two (2) copies of the Informed Consent form need to be signed by the Coordinator/RA and patient. Once Informed Consent is obtained, range of motion and strength measurements will be performed by study staff. The patient will then be given the study questionnaires and given the option to complete them in the waiting room or mail them back to us in a pre-paid addressed envelope. If the patient elects to return the questionnaire in a pre-paid envelope, the Coordinator/RA will have the patient fill out the "05. Patient Information" form so that the patient can be reached if we do not receive the questionnaires within one week. Up to three (3) calls will be made by the research assistant if the questionnaires are not returned. Eventually if the

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questionnaire is still not returned after 3 phone calls by the research assistant, the PI will make one (1) final phone call. Our phone call protocol for return of baseline questionnaires is outlined in the document "ROW BASELINE PHONE CALL SCHEMA". All history and standardized questionnaires used for our study are included in the documents "02. Screening Form Left/Right_4", "05. Patient Information", "06. NEW History Form_1", "07. NEW AM-PAC_Shoulder Short Form", 07. NEW Standardized Questionnaires_1", and "09. Degree of certainty form_4". The patient will also be asked about their willingness to be randomized in a hypothetical randomized clinical trial if there were one today using the questionnaire and script included in the documents entitled "ROWr Patient Randomization Script" and "12. ROWr Questionnaire for ROW patients". Please note that this is not a randomized trial and no patients will be randomized. Their care will proceed as usual care prescribed by their physician. The patient also undergoes range of motion and strength testing and foms used for this purpose are included in the document, "08. Physical Examination Form". The protocol for strength and range of motion measurement is included in the document "ROM Dynamometry Protocol".

Imaging Assessment, Intra-Operative Findings, and Follow-Up

Once the patient is recruited, the study investigators will independently assess the patient's MRI in a blinded manner so as to confirm that the patient indeed has a rotator cuff tear and complete the "MRI Reading Form_4". If the patient is not found to have a rotator cuff tear on the blinded independent MRI review, the patient will be excluded from the study. The patient will be mailed a letter of exclusion and the patient's attending physician will be informed via email that the study investigators concluded that the patient did not have a rotator cuff tear based on their reading of the images. A sample letter for patient exclusion is included in the document "Letter for Patient Exclusion".

If a study subject undergoes surgery for their rotator cuff tear, their attending surgeon will also fill out the "RCR Data Collection Form_2" which provides details on intra-operative findings.

Patients are followed at 3, 6, 12, 18, 24 months and yearly thereafter, up until Year 10. All follow-ups are conducted via questionnaires and our protocol to obtain follow-up questionnaires from patients are outlined in the document "ROW FOLLOW UP PHONE CALL SCHEMA". If patients are emailed for follow-up questionnaires (instead of phone calls), a standardized script for the same is available in the document, "Email Script". All follow-up questionnaires are included in the documents "02. Surgery Update Form", "04. Patient Information", "05. NEW Follow-up History Form Follow Up_1", "06. NEW Standardized Questionnaires Follow Up", "07. NEW AM-PAC_Shoulder Short Form", and "08. NEW PT Follow Up_1".

B. Identify the criteria for inclusion and exclusion and explain the procedures that will be used to determine eligibility. If psychiatric/psychological assessments will be conducted (e.g., depression or suicidal ideation screenings), state who will administer, his/her experience, and how risks will be managed.

Eligibility Criteria: Patients must meet all of the following criteria:

- Age 45 or older and be diagnosed with an atraumatic rotator cuff tear
- Symptoms for at least 4 weeks of shoulder pain and/or limitation in range of motion of shoulder

Exclusion Criteria: Patients are excluded if they meet any of the following criteria:

- History of shoulder and humeral fractures
- Prior surgery on the same shoulder
- Contraindications to MRI (prior surgical hardware, pacemakers, defibrillators, and claustrophobia)
- Unable or unwilling to give informed consent
- Unable or unwilling to be followed up
- Non-English speaking (as questionnaires have only been validated in English)

Patients agreeing to participate in our study will be consented for the study by a trained Research Coordinator/Research Assistant. The informed consent will be performed in a separate examination room in the clinic. The patient will be given the option of deferring the decision to participate in the study until they have had

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more time to go over the consent form. A phone number for study staff will be provided in this case so that the patient can obtain additional information if need be.

C. Describe how the selection of participants is equitable in relation to the research purpose and setting *(e.g., no one ethnic group is targeted or excluded, the same group of participants will benefit from the results of the research)*. Describe the composition of anticipated participants such as teachers, students, parents, etc.

No one ethnic group will be targeted or excluded, as the same group of participants will benefit from the results of this research. All patients, regardless of gender, race, or ethnicity are included if they fit the inclusion criteria and agree to participate. However, children will be excluded since the pathophysiology of rotator cuff tears in children is usually traumatic and not degenerative.

1. Please indicate whether you plan to enroll any of the populations listed below:

- ☐ VU Medical Students
- ☐ Elderly/Aged - targeted
- ☐ Females of childbearing potential
- ☐ Healthy volunteers
- ☒ Other, specify: Patients with rotator cuff tears
- ☐ Students
- ☐ Subordinates/Employees
- ☐ Terminally ill participants
- ☐

E. Please identify ALL applicable recruitment methods: ***NOTE: Please provide an approved copy of all advertising materials including ads, letters, and telephone scripts with this application (must include graphics). In addition, the IRB must review and approve final copies of all audio and videotapes prior to use.***

☐ Not Applicable; or

Choose all that apply:

- ☐ Flyers
- ☐ Internet
- ☐ Letter
- ☐ Departmental Research Boards
- ☐ Other (describe):
- ☐ Mass E-mail Sollicitation
- ☐ Newspaper
- ☐ Posters
- ☐ ResearchMatch (IRB 090207)
- ☐ Radio
- ☒ Telephone
- ☐ Television
- ☐ Social Media

F. Compensation: Specify the method of compensation (e.g., money, gift certificates, prizes, toys, etc.). If payment schedules are complex, it is suggested that a table is included showing the frequency and amount of compensation.

Participants will be provided $50 remuneration for completing baseline study procedures (physical exam, range of motion and muscle strength measurements, questionnaire completion). Participants will be compensated $25 for each questionnaire completed at 3, 6, 12, 18, 24 months and annually up to 10 years. Thus, participants may receive up to $375 if you complete all parts of the study.

Compensation will be provided after receipt of completed questionnaires by study staff at Vanderbilt.

E. Will compensation or reimbursement (cash or items of value) be provided to participants?

- ☐ No
- ☒ Yes

If "*Yes*", you are required to collect a social security number from each participant. If recording the social security number of the participant confers added risk (other than the typical financial risks associated with inappropriate disclosure of a SS#) or is likely to significantly impair participant enrollment, you may request exception to the requirement for collection of SS#. Exceptions will be evaluated on a case by case basis but will be granted only if

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participants aggregate income in any calendar year from all Vanderbilt sources (e.g. participant is involved in multiple studies or is a Vanderbilt employee or vendor) will be less than $600.

F. Do you wish to have your study evaluated for SS# documentation exception?
☒ No
☐ Yes
You must have IRB approval as well as a separate SS# exception approval before reimbursing participants without documenting the SS#. If you indicate yes, the exception project manager may contact you via email within approximately 2 weeks to provide additional information. You may not begin engaging participants in research without collecting SS#s until you receive an email notification of SS# exception approval (separate from IRB approval). SS# exceptions will not be granted for Vanderbilt employees who are participants.

G. Do you agree to release study information to Vanderbilt-approved list services, web sites or publications? (Vanderbilt has a variety of list services and publications, such as the Clinical Trials Website. Posting research protocol information on research-related websites and other listing services, allows potential participants to search and find studies related to their condition or interest. ***(Please be aware that if this research is subject to a contractual agreement, it may be necessary for you to obtain permission from the sponsor prior to authorizing the release of any study information.)***
☒ No, do not release information to research-related web sites and other listing services.
☐ Yes, this information may be released as described in the lay summary.

H. Does this study require registration with Clinicaltrials.gov? ***Please be aware there are four mandates that require registration of clinical trials and as the Principal Investigator for this study, it is your responsibility to assure proper registration of your trials. Failure to comply with applicable rules and guidance can result in serious penalties as well as restrictions on publications. In general, only some phase I clinical trials are exempt from registration. Click on the help buttons above for further information.***

☒ No *If "No", please provide a rationale of why registration is not required.*

As this is an observational longitudinal cohort study, this does not require registration with Clinicaltrials.gov.

☐ Yes *If "Yes", do you have the National Clinical Trials (NCT) Registry Number?*
☐ Yes, NCT Number:
☐ No, ***Submit the number through DISCOVR-E once received.***
☐ N/A, *the sponsor of this study will register the trial.*

SECTION 7:

16. Methods and Procedures Applied to Human Participants (check all that apply)

A. Have you attached a research protocol that includes a description of the following: background, rationale and specific aims, inclusion/exclusion criteria, enrollment/randomization, study procedures, adverse event reporting, study withdrawal/discontinuation, statistical considerations, privacy/confidentiality issues, follow-up, and record retention?
☐ No If *"No," please complete and attach a research protocol that addresses the above criteria, as applicable.*
☒ Yes

B. ☐ **Behavioral Observation**
Describe the focus, duration, and number of observations and specify how the observations will be recorded.

C. ☐ **Randomization**

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D. ☐ **Blinding**

Describe who will be blinded. Describe if and when research results or previously blinded treatment assignments will be made available to participants. Describe the provisions for breaking the blind (e.g., emergency situations, participant's request, etc.).

C. ☒ **Surveys, Interviews, Questionnaires**

If surveys, interviews or questionnaires will be conducted with this study, indicate who will conduct the survey, interview or questionnaire and their qualifications. In addition, describe the setting and mode of administering the instrument (e.g., by telephone, one-on-one, group, etc.) and attach a copy of the instrument.

Patients agreeing to participate in our study will be consented for the study by a trained research coordinator / research assistant. The informed consent will be performed in a separate examination room in the clinic. The patient can fill out study questionnaires in the waiting room or mail them back to us in a pre-paid addressed envelope.

G. ☒ **Document and Artifact Collection**

Describe any documents or other artifacts (e.g., student written assignments, EKG report, x-rays, etc.) that are to be collected.

Standard of care MRIs, ultrasounds, and x-rays will be collected, if ordered for clinical purposes. X-rays will not be performed for research purposes.

H. ☐ **Specimen Collection (If you are also building a repository, answer questions iii.1-5 below, otherwise skip to I.**

i. Blood drawing (indicate total amount drawn for research purposes).
ml over period.
Note: Please include description in consent document referencing amounts of blood in teaspoons, tablespoons or pints.

ii. Other specimens (describe the type of specimen and frequency of collection).

iii. Will specimens be obtained for genetic testing in association with this study or will they be stored for future research use?
☐ No
☐ Yes *If "Yes", include genetic template language in the informed consent document. Complete 1-5.*

1. *Specify the types of tissue or data to be banked. Describe the source of the data or specimens and the tools that will be utilized in the collection and storage of research information.*

2. *Are the specimens/data identified/coded?*
☐ *No* ☐ *Yes*
Note: If identifiers are used and the data or results could adversely affect the participant or family, now or in the future, a Certificate of Confidentiality is recommended.

3. *Describe the procedures that will be used to de-identify specimens/data, if applicable.*

4. *Describe the management of the Repository including:*

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- *The identity of the person responsible for maintaining the Repository and the identity of any others involved with stripping identifiers, coding or distributing samples/data;*
- *What will happen to specimens if the PI leaves the institution; and*
- *What will happen if an individual decides to withdraw consent.*

(Please be aware that all specimens and data collected with the use of University facilities or funds administered by the University are the property of Vanderbilt University. Please reference the Vanderbilt University *Faculty Manual*, 2003 Edition, Chapter 4, Section B. Specimens and data may not be removed from the University without the prior approval of the IRB and the Faculty Member's Dean and Chair.)

5. *Describe the storage facilities and tracking system to be used, including how the specimens/data are received, accessed and released.* ***(Please be aware it is the PI's responsibility to assure that specimens/data are only released to projects with specific IRB approval for their use.)***

I. ☐ **Deception, Withholding or Postponing Medications/Treatments, or Imposing other Restrictions**

Describe the methods of deception to be used, the medications being withheld or postponed, the length of time medications will be withheld or postponed, any other restrictions to be imposed on participants (i.e., diet, exercise), and the precautions taken to decrease or eliminate risks to participants.

J. ☒ **Data Collection, Storage of Data/Specimens and/or Issues of Confidentiality**

NOTE: Any device (e.g., personal computer, laptop, etc.) used to save or store individually identifiable health information must be either encrypted or saved on a server housed in an approved data center. Vanderbilt Medical Center has agreed to use Check Point. For more information and how to obtain Check Point please visit the website: Information Privacy and Security.

i. Describe the tools that will be utilized in the collection and storage of research information including data (hard copies and electronic databases, specimens, audio/videotapes, etc.). Indicate who will have access to the research information and describe the final disposition of research information when the study is concluded (e.g., will information be destroyed or will the PI maintain the information).

Hard copies of patient study questionnaires and collection forms, physician study collection forms, and imaging forms will be collected and stored in locked file cabinets contained with the Departments of Orthopaedics and Physical Medicine and Rehabilitation. Only approved research staff will have access to the key. Data will be electronically stored in REDCap, where only study-related personnel will have access.

The study PI will maintain all study-related documents and information (it will not be destroyed).

ii. Describe how the confidentiality of participants will be assured. Include a description of any issues specific to the study that might increase the risk of breach of confidentiality. For example, video/audiotapes, discovering information about the participant that could be harmful if released such as mental illness, genetic information, sexual preference, drug abuse, etc. Describe how codes will be generated if codes are used to protect identities, and who will have access to such codes. If a certificate of confidentiality will be provided, include the name of the person holding the certificate.

All efforts, within reason, will be made to keep the patient's protected health information (PHI) private. Upon being enrolled in the study, each patient will be given a unique study ID. This study ID is generated with the prefix 3-1-xxx or 3-2-xxx. This de-identified study number will be used for all data analysis. Only the study staff will have access to the codes.

K. ☐ **Audio or Video Taping**

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i. Describe how the audio/videotapes will be stored.

ii. Describe how the tapes will be disposed of when this research is complete.

iii. Describe how the participant's confidentiality will be maintained.

17. Schedule of Events and Research Procedures for Study Participants

A. Complete the table below, indicating research activities and procedures only. ***(Limit list to research activities and procedures, excluding standard of care procedures and activities even if they are included in the protocol.)*** Table may be modified as necessary to accommodate more items.

Procedure/Activity	Frequency
Patient Questionnaire	Baseline 3, 6, 12, 18, 24 months Years 3,4,5,6,7,8,9,10
Research Physical Exam (strength, range of motion measurements)	Baseline

B. Will there be costs generated in this study at Vanderbilt?

(Examples: Any tests, interventions, and/or procedures that are billed to a D&H account, patient insurance, sponsor, departmental funds, or other 3rd party.)

☒ Yes If "Yes," complete the charge intention in StarBRITE.
Please contact the Office of Contracts Management for questions.

☐ No If "No," continue to C.

☐ N/A There are no procedures that involve interaction or intervention with participants or generate costs in this study (e.g., data collection/analysis only, chart review).

C. Will there be costs generated in this study at **non-**Vanderbilt sites?

(Examples: Enrollment at VICCAN affiliated sites where the VU IRB is the IRB of record; Vanderbilt is the coordinating center but there will be no accrual at Vanderbilt; any tests, interventions, and procedures done at non-Vanderbilt sites and the VU IRB is the IRB of record.)

☐ Yes If "Yes," attach a ***completed*** Research Procedure Supplemental Form #1140 in DISCOVR-E.
☒ No.

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SECTION 8:

18. Consent:

Describe the specific steps for obtaining informed consent and the procedures that will be utilized to protect the privacy of individuals (e.g., by whom, his/her credentials, where consent will be obtained, when, etc.)

Patients agreeing to participate in our study will be consented for the study by a trained research coordinator / research assistant. These individuals have experience in enrolling patients, and have undergone Vanderbilt's Research Support Services "Boot Camp".

The informed consent will be performed in a separate examination room in the clinic. The patient will be given the option of deferring the decision to participate in the study until they have had more time to go over the consent form. A phone number for study staff will be provided in this case so that the patient can obtain additional information if need be. If the patient agrees to receive more information, the study's research coordinator / research assistant will explain the study to the patient using the "Patient Recruitment Script" (see attached).

Does the person obtaining consent have an existing relationship with the participant(s)?

☒ No
☐ Yes *If "Yes", indicate describe the relationship(s) and how you will protect against undue influence or coercion.*

Describe any planned waiting periods between informing potential participants of the research and obtaining consent, if applicable.

There is no planned waiting period between informing potential participants and obtaining consent. However, as mentioned above, the patient has the opportunity to take home all the information and call us back if additional questions arise.

19. Will surrogate consent be requested?

☒ No
☐ Yes *If "Yes", indicate rationale for use of surrogate consent.*

20. How will non-English speaking participants be consented? ☐ **Requesting waiver only** *(skip to #21)*

(Federal regulations require the equitable selection of minorities as research subjects to assure that they receive an equal share of the benefits of research and to ensure that they do not bear a disproportionate burden.)

A. Choose one:

☐ A translated written informed consent document in a language understandable to the participant. This should be an accurate translation of the full informed consent document *(consider having a translator present during the consenting process should the participant have any questions).*

☐ Orally, using a qualified translator to translate the English informed consent document to the participant, and a translated short form in a language understandable to the participant. (*See* "Documentation of Informed Consent" at IRB Policy IV.B for details).

☒ If only enrolling English speaking participants, provide justification:

The standardized questionnaires used in this study are available and validated in English. Hence, non-English speaking patients will not be enrolled in this study.

B. Identify the name of the individual or translation service that provided the translation.

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C. List the qualifications of the individual that provided the translation.

21. Will a waiver or alteration of the consent process or a waiver or alteration of the consent documentation be used?

☒ No
☐ Yes *If "Yes," please complete the Request for Waiver of Consent and/or Authorization*

Please refer to IRB Policy IV.C for further guidance. Please be aware, if a protocol is granted a "Waiver of Consent and/or Authorization" by the VU IRB, and the study involves the use of PHI, the PI is responsible for accounting of disclosures. Please contact the Vanderbilt Privacy Office at: http://www.mc.vanderbilt.edu/root/vumc.php?site=HIPAA, or call 936-3594.

22. Will Protected Health Information (PHI) be accessed (used) in the course of screening/recruiting for this research?

☐ No
☒ Yes *If "Yes", the following 4 conditions must be met:*

1. The use or disclosure of the PHI is sought solely for the purpose of this research protocol.
2. The PHI will not be removed from the covered entity. *See "The Statement of Hybrid Designation"* for the definition of the Covered Entity.
3. The PHI is necessary for the purpose of this research study.

Use or Disclosure of Protected Health Information

Does this research use or disclose Protected Health Information (PHI)?
Protected health information (PHI) is individually identifiable health information that is or has been collected or maintained by Vanderbilt's Covered Entity, including information that is collected for research purposes only, and can be linked back to the individual participant.

☐ No
☒ Yes *If "Yes", please continue:*

i. Indicate the source of the PHI to be collected (e.g., medical records, specimens, data previously collected for research purposes).
Starpanel/Epic (medical records)

ii. Indicate when PHI will no longer be accessed (e.g., closure of study, destruction of database, no expiration).
Closure of the study.

Identify all Non-VU affiliated Individuals/Institutions (those that are outside the covered entity) to which PHI may be disclosed (e.g., study sponsors, CRO's, consulting physicians, publications, future collaborators, etc.):

Name of Institution and/or Individual	Data Use Agreement Required?
	☐ Yes ☐ No
	☐ Yes ☐ No

SECTION 9:

23. Use of Drugs, Devices, Biologics, and Gene Transfer ☒ N/A, skip to B

A. ☐ FDA-approved Drug(s)/Biologic(s) Used for Research [only include drugs that are being used outside of package insert labeling for indication, route of administration, dose, dosing frequency, dosage form, and/or population in which the drug is being used (i.e. children)]

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i. Identify the name of all of the FDA-approved drug(s)/biologic(s) used for research in this protocol along with a description of the dose range, frequency, the population it is used in, route of administration and source.

ii. Please answer the following questions for each drug listed above in section 21.A.i. If answering "YES" for any of the questions, please indicate to which drug(s) the answer applies on the space provided.

a. Are you intending to report the study results to the FDA to support a new labeling indication or labeling change?
☐ Yes ☐No If "YES", which drug(s)?_____

b. Are you intending to report the study results to the FDA to support a change in the advertising?
☐ Yes ☐No If "YES", which drug(s)?_____

c. Does the planned use of the study drug increase the risks or decrease the acceptability of the risks to the subjects participating in the study?
☐ Yes ☐No If "YES", which drug(s)?_____

d. Does the study require any change in the approved formulation, dosage level, population, or route of administration of the drug?
☐ Yes ☐No If "YES", which drug(s)?_____

NOTE: If the responses to a-d above are all "NO," the clinical investigation of the marketed drug or biologic may be considered IND Exempt. If not IND exempt, a written determination from the FDA is required. Skip to B.ii of this application.

iii. Describe how the drug(s) will be handled, stored, and dispensed.

24. ☐ Investigational (Non-FDA approved) Drug(s)/Biologic(s) used for Research ☒ N/A, skip to C

NOTE: Investigator-sponsors who will hold the IND for the study drug(s) must complete and submit the Supplemental Form for Investigator Held IND(s), IRB Form # 1135.

i. Identify the name of all of the Investigational Drug(s)/Biologic(s) listed in the protocol along with a description of dose range, frequency, route of administration and source.

ii. IND number assigned by FDA **(Copies of all completed 1572s as well as documentation of FDA approval for the use of the agent(s) must be provided for IRB review)**.

iii. Who holds the IND?
☐ Sponsor
☐ PI ***Complete the Supplemental Form for Investigator Held IND(s) # 1135***
☐ Cross-referencing another IND ***Complete the Supplemental Form for Investigator Held IND(s) #1135 and Include the "Letter of Authorization" to Cross-Reference***

iv. Are other research studies using this IND?
☐ No
☐ Yes *If "Yes", please list IRB #(s):*

v. Will the Investigational Pharmacy be dispensing the drug(s)/biologic(s)?
☐ No
☐ Yes

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a. Identify the name of the Manufacturer or source of investigational drug(s)/biologic(s).

b. If the source is not a FDA licensed facility, provide details regarding the purity, quality, stability and sterility of the investigational drug(s)/biologic(s).

c. Identify who will be preparing the investigational drug(s)/biologic(s), their qualifications, and describe how it will be prepared in detail. **Note: If the drug(s) will be compounded by the Investigational Drug Service (IDS), attach the approved compounding formula. For more information, call the IDS at 343-6537.**

d. Describe how the investigational drug(s)/biologic(s), will be handled, stored, and dispensed. **Note: If the drug(s) will be handled, stored, and dispensed by the Investigational Drug Service (IDS) simply state "Contracted with VU Investigational Drug Service (IDS) for this service."**

☐ **Placebo-controlled (inactive substances and/or sham products and/or procedures)**

If an "inactive substance" will be used in the study, identify the name of the inactive ingredient along with a description of the dose range, frequency, route of administration and source.

1. Identify who will be preparing/providing the placebo.

2. Provide the details regarding the purity, quality, stability and sterility of the placebo and/or inactive ingredients.

If a sham product and/procedure will be used in this study please describe:

C. ☐ Device Use. ***(If a device is being used for research please complete the Supplemental Form for Use of Devices in Research, IRB Form#1134, for submission with this application.)***

D. ☐ Gene Transfer (***Note: If any answer in this section is checked yes, approval from the Institutional Biosafety Committee is required.)***

i. Does this study involve the deliberate Transfer of Recombinant DNA, RNA, or DNA or RNA derived from Recombinant DNA into one or more human subjects?
☐ No ☐ Yes

ii. Does this study utilize Live, Recombinant, and/or Attenuated Microorganisms for Vaccination of one or more human participants?
☐ No ☐ Yes

iii. Does this study utilize a Select Agent as defined by the CDC in 42 CFR 72 (see page 14)?
☐ No ☐ Yes

SECTION 10:

23. Additional VU Committee Approvals *(check all that apply)*: ☒ **N/A**

☐ *Institutional BioSafety Committee (IBC) Approval Date:

☐ *Radioactive Drug Research Committee (RDRC) Approval Date:

☐ Scientific Review Committee (SRC) Approval Date:

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Copy of approval letter required before final IRB approval will be extended.

24. Potential Conflict of Interest

A. Is there a potential conflict of interest for the Principal Investigator or key research personnel?

- **The PI is responsible for assuring that no arrangement has been entered into where the value of the ownership interests will be affected by the outcome of the research and no arrangement has been entered into where the amount of compensation will be affected by the outcome of the research.**
- **Assessment should include anyone listed as Principal Investigator, or other research personnel on page 1 of this application. Please note that ownership described below apply to the aggregate ownership of an individual investigator, his/her spouse, domestic partner and dependent children). Do not consider the combined ownership of all investigators.**

☒ No
☐ Yes *If "Yes", the investigator must complete and submit IRB Form #1120, "Conflict of Interest Supplemental Form" with this application. Form #1120 and the protocol must be reviewed by the VU Conflict of Interest Committee*.

NOTE: The Investigator may not proceed with the research until a final determination letter has been rendered by the MCCOIC or the University Conflicts Committee and IRB approval has been granted.

B. *If "Yes", check all that apply*:

☐ Compensation whose value could be affected by the study outcome.

☐ A proprietary interest in the tested product included but not limited to, a patent, trademark, copyright or licensing agreement, or the right to receive royalties from product commercialization.
If "yes," are these distributed through the Vanderbilt Center for Technology Transfer and Commercialization?
☐ No
☐ Yes

☐ Annual income (e.g., consulting fees, honoraria, paid authorship) and/or equity interest (e.g., stock, stock options) in the sponsor or product valued in excess of $5,000.

☐ Any equity interest in the sponsor (e.g., stock or stock options, founders' share) if a non-publicly traded company.

Informed Consent Document Templates

Download from http://www.mc.vanderbilt.edu/irb/forms/ then save and submit as a separate file from the IRB Application.

Submit the following to the IRB: the original Application for Human Research and any additional background information (Investigator's brochure, sponsor's protocol, dissertation, grant). To facilitate the review and revision process electronic versions of all documents will be requested once the study is assigned to a team.

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