IRB #: _____
(Assigned by IRB Office)

CPA #: _____
(Assigned by IRB Office)

***Form Directions**: Form is protected (user has limited access to the fill-in fields). Use the tab key or mouse to navigate the fill-in fields. Formatting is limited in the text fields (no bulleted lists, numbering, etc). In the event that the user is unable to navigate through the protected document or would like to format a document, the user can disable the "protected" feature (select "Review" then "Restrict Ending" then "Stop Protection"). Please do not delete or modify questions..*

Louis Stokes Cleveland Department of Veterans Affairs Medical Center Research Plan

Please contact the IRB office if you have any questions at (216) 791-3800 ext. 64658.

☐ **Request for Expedited IRB Review Form attached**

Human Subject Research: Human subject research means research involving interaction or intervention with living human beings or access to identifiable private information of living human beings.

Research Plan: The information requested in the Research Plan is designed to provide the IRB with the necessary information such that it can make the federally required determinations codified at 38 CFR Part 16, 21 CFR Parts 50, 54, & 56, and 45 CFR Part 46

The **Research Plan** is to be written so that the non-scientist/non-medical members of the IRB can understand the research proposed. Define all abbreviations and terms that are not part of common language.

Version Date: This should be updated subsequently with every modification to any part of the Research Plan. Any modification to this document, no matter how minor, must be reviewed and approved by the IRB prior to implementation. The Research Plan will be stamped with the date of IRB approval

.

Section 1 – General Information

1. Version Date: August 31, 2023

2. Title of Project: Computerized game-based vestibular rehabilitation: assessment of feasibility and motor learning

3. Principal Investigator (PI) *(name & degrees)***:** Mark Walker, M.D.

E-mail: mark.walker5@va.gov

Pager Number/Cell Phone Number: 440 562 0458

4. Research Contact/Research Coordinator *(name, degrees)***: n/a**

E-mail:

Pager Number/Cell Phone Number:

Section 2 – Research Sites and Sponsor

5. Please list all Research Sites in addition to Louis Stokes Cleveland DVA Medical Center (LSCDVAMC); n/a

International studies when the PI is the Lead Investigator list the countries: n/a

a. When study procedures including analysis of identifiable samples or data involving LSCDVAMC enrolled subjects will be conducted at any site other than the LSCDVAMC please provide the following:

Name and contact information for the site: n/a

Describe the plan for communicating protocol amendments, reports of serious adverse events, reports of unanticipated problems involving risks to subjects or others, interim reports, and DSMB reports to external sites. n/a

*** When the LSCDVAMC is considered the coordinating center and the PI the lead investigator on cooperative research or a multi-center trial contact AO/Research Holly.Henry@va.gov.**

6. Sponsor or other Support *(list industry sponsor, government support, etc.)*:

VA RRD

Section 3 – Research Design and Procedures

7. Definitions- Provide a list of all abbreviations and specialized terms to be used in this document and their definitions:

Abbreviations / Specialized Terms *(Use the Enter key in this column to insert additional abbreviations and their definitions)*	**Definition**
LSCDVAMC	Louis Stokes Cleveland DVA Medical Center
VOR	Vestibulo-ocular reflex
DVA	Dynamic visual acuity

8. Provide a BRIEF SUMMARY of the background for this research. DO NOT CUT and PASTE paragraphs that do NOT summarize the background.

- *Include a critical evaluation of existing knowledge, and specifically identify the information gaps that your protocol is intended to fill.*
- *Refer to appropriate citations in the scientific literature and include your references at the end of this section.*
- *Include the rationale for conducting the research at the VA.*

The overall goals of our research are to understand how the brain processes visual and vestibular signals to drive eye movements and postural reflexes, how these functions are disturbed in neurological diseases, how those disturbances cause functional impairments for patients, and how these problems can be treated. The goal of this project is to test the

efficacy of a custom computer game to induce motor learning in the vestibulo-ocular reflex (VOR) and to obtain preliminary data of its feasibility as a tool for clinical vestibular rehabilitation. Vestibular disorders occur commonly in the general population, including veterans, and they are associated with reduced quality-of-life, disruption of work, and limitations of independence [1-4].

Vestibular rehabilitation is the mainstay of treatment for these conditions [5, 6], but standard therapy has key limitations and cannot be easily customized to each patient's specific level of functional impairment. This project builds on our preliminary work to develop an interactive computer game for customized vestibular rehabilitation in clinical and home settings.

Traditional vestibular rehabilitation [7] and our new approach are based on research regarding vestibular physiology and the plasticity of the VOR[8-12]. The primary function of the VOR is to compensate for head movements by rotating the eyes in the opposite direction to stabilize the retina on the object being viewed. This permits vision to remain clear during movement. When vestibular function is lost due to disease, the VOR no longer functions properly and gaze stability during head movement is lost. Vestibular rehabilitation aims to retrain the VOR by improving the function of the reflex and facilitating the optimization of alternative motor strategies to aid compensation.

Recent work suggests that incremental VOR adaptation may be more effective than single-step adaptation[13]—it may be easier to adapt stepwise to smaller errors than to a large error all at once. This approach involves gradually increasing the amount of scene motion relative to the head as the VOR adapts, always working closer to the current level of function. The ability to adapt the VOR incrementally is a key aspect of our vestibular game, and the effectiveness of this approach for short-term adaptation will be directly tested in Aim 1.

1. Agrawal Y, Carey JP, Della Santina CC, Schubert MC, Minor LB. Disorders of balance and vestibular function in US adults: Data from the national health and nutrition examination survey, 2001-2004 Arch Intern Med 2009;169:938-944.

2. Neuhauser HK, Radtke A, von Brevern M, Lezius F, Feldmann M, Lempert T. Burden of dizziness and vertigo in the community Arch Intern Med 2008;168:2118.

3. Agrawal Y, Ward BK, Minor LB. Vestibular dysfunction: Prevalence, impact and need for targeted treatment J Vestib Res 2013;23:113-117.

4. Ward BK, Agrawal Y, Hoffman HJ, Carey JP, Della Santina CC. Prevalence and impact of bilateral vestibular hypofunction: Results from the 2008 US national health interview survey JAMA Otolaryngol Head Neck Surg 2013;139:803-810.

5. Cooksey FS. Rehabilitation in vestibular injuries Proc R Soc Med 1946;39:273-278.

6. Hall CD, Herdman SJ, Whitney SL, et al. Vestibular rehabilitation for peripheral vestibular hypofunction: An evidence-based clinical practice guideline. Journal of Neurologic Physical Therapy 2016;40:124-155.

7. Herdman SJ. Role of vestibular adaptation in vestibular rehabilitation Otolaryngol Head Neck Surg 1998;119:49-54.

8. Rambold H, Churchland A, Selig Y, Jasmin L, Lisberger SG. Partial ablations of the flocculus and ventral paraflocculus in monkeys cause linked deficits in smooth pursuit eye movements and adaptive modification of the VOR. J Neurophysiol 2002;87:912-924.

9. Miles FA, Lisberger SG. Plasticity in the vestibulo-ocular reflex: A new hypothesis. Annu Rev Neurosci 1981;4:273-299.

10. Boyden ES, Katoh A, Raymond JL. Cerebellum-dependent learning: The role of multiple plasticity mechanisms. Annu Rev Neurosci 2004;27:581-609.

11. Luebke AE, Robinson DA. Gain changes of the cat's vestibulo-ocular reflex after flocculus deactivation. Exp Brain Res 1994;98:379-390.

12. Luebke AE, Robinson DA. Climbing fiber intervention blocks plasticity of the vestibuloocular reflex. Ann N Y Acad Sci 1992;656:428-430.

13. Schubert MC, Della Santina CC, Shelhamer M. Incremental angular vestibulo-ocular reflex adaptation to active head rotation. Exp Brain Res 2008;191:435-446.

9. Provide a BRIEF SUMMARY of the purpose and scientific rationale for this research. DO NOT CUT and PASTE paragraphs that do NOT summarize the purpose and scientific rationale.

- *State clearly, in terms a non-scientist/non-medical person can comprehend, what you expect to learn from the study and the specific hypothesis (es) to be tested.*
- *The objectives should be stated in such a way that the reader can determine the appropriateness of the study design.*

The hypothesis of the study is that computer-game-based incremental adaptation will induce robust VOR motor learning and will provide an engaging platform for vestibular rehabilitation.

In the first aim, we will test the ability of the game to induce VOR plasticity (to modify the gain of the VOR) in subjects with intact vestibular function. To do this, we will have subjects play the game with a visual condition (background movement that is tied to head velocity) that requires them to make a larger than normal eye movement when the head rotates. Such visual-vestibular mismatch has been shown in the past to lead to an increase in the gain of the VOR, even when tested in the dark. Our hypothesis is that incremental adaptation (increasing the amount of visual-vestibular mismatch gradually in a series of steps) will be more effective in inducing this plasticity, so we will compare the change in gain with this paradigm to that induced by imposing the full amount of visual-vestibular mismatch all at once.

In the second aim, we will obtain preliminary data regarding the efficacy and feasibility of the game for clinical vestibular rehabilitation. Patients with peripheral vestibular hypofunction will play the game with the degree of visual-vestibular mismatch customized for their individual level of impairment. They will provide feedback regarding the game and their tolerance of the playing experience. Each subject will play once a week for four weeks. This will give us preliminary data regarding short-term VOR learning in these patients.

10. Describe the means of analyzing the data and evaluating the results.

- *State the anticipated methods to be used for analysis and interpretation of the data.*
- *The methods must compliment the design of the study and the nature of the data which is being collected.*

Data Analysis: The primary outcome measures for this experiment are the passive and active VOR gains. The VOR gain will be calculated for each subject and condition using an

optimization procedure in MATLAB that fits eye velocity to delayed head velocity. In addition to assessing the slow-phase gain change, we will examine “non-vestibular” components of the post-adaptation eye movements; for example, an increase in saccades during the head rotation (covert saccades) may also contribute to gaze stability.

A secondary measure will be the change in DVA with x1.5 viewing, with the prediction that DVA with the moving scene will improve after the VOR has adapted to that visual-vestibular condition and that the improvement in DVA will correlate with that of the VOR. Pre- and post-adaptation VOR gains will be compared using a paired t-test, employing a power transformation if the assumption of normality is not satisfied. Most of the software that will be required for data analysis has already been written by the PI or other members of the laboratory.

Vestibular patients will complete questionnaires (Dizziness Handicap Inventory, Activity-based Balance Confidence) to assess the extent and functional impact of their symptoms, but these will not be outcome measures for the study.

Subjects will rate their feelings of motion sickness on a 0-10 scale following each playing session.

11. Provide a BRIEF DESCRIPTION of how the estimated number of study subjects needed for this research was determined

- *If this is a quantitative study provide the method of determining sample size estimates.*
- *If multiple studies are planned provide a power analysis or justification for each one*.

This is an unpowered pilot study that is funded under the SPiRE mechanism. The number of subjects was chosen to provide adequate preliminary data to support a funding application for a larger clinical trial.

12. The research involves the following procedures conducted by and for what purpose:

PROCEDURE	PERFORMED BY:		PROCEDURE IS:	
	Research Staff	LSCDVAMC Clinical or Support Staff	Standard of Care*	For Research Purposes Only**
Audiotaping / Videotaping *Attach VA Form 10-3203* **REQUIRED ONLY FOR IN-PATIENT AND OUT-PATIENT SUBJECTS**	☐	☐	☐	☐
Biopsy	☐	☐	☐	☐
Blood collection	☐	☐	☐	☐
Chart review – prospective	☒	☐	☐	☒
Chart review – retrospective	☒	☐	☐	☒
Review of existing data (ex: registry, Database , etc.)	☐	☐	☐	☐

PROCEDURE	PERFORMED BY:		PROCEDURE IS:	
	Research Staff	LSCDVAMC Clinical or Support Staff	Standard of Care*	For Research Purposes Only**
X-ray or Ionizing radiation exposure	☐	☐	☐	☐
Clinical Tests	☒	☐	☐	☒
Device implantation	☐	☐	☐	☐
Drug administration	☐	☐	☐	☐
EEG, EKG , ECG…etc	☐	☐	☐	☐
Gene therapy, Genetic analysis	☐	☐	☐	☐
Pregnancy/Breastfeeding Screening	☐	☐	☐	☐
Interview, Questionnaire, Diary, Survey *(please attach)*	☒	☐	☐	☒
Stool collection, Urine collection, or any Non-surgical Specimen collection	☐	☐	☐	☐
Surgical procedure or Specimen removal during surgery	☐	☐	☐	☐
Tissue banking *(complete Section 12)*	☐	☐	☐	☐
Use of pre-existing tissues/specimens	☐	☐	☐	☐
Other *(list)***:** measurement of head and eye movements; measurement of visual acuity; exposure to visual stimuli during passive and/or active head movement, including while playing a video game.	☒	☐	☐	☒

- **Standard of care procedures are procedures performed in the course of normal medical care.*
- ***Research Procedures are performed for the purposes of this research alone.*

13. Please describe the research design and all study related procedures.

- *Describe **ALL PROCEDURES ASSOCIATED WITH THIS RESEARCH**. This includes standard of care and research procedures.*
- *For complex studies please include diagrams and tables. Be sure to describe when each procedure will be performed. Be sure to provide information for **each cohort, including normal controls**).*

The hypothesis of the study is that computer-game-based incremental adaptation will induce robust VOR motor learning and will provide an engaging platform for vestibular rehabilitation. The hypothesis will be tested with two specific aims:

Aim 1 (Healthy volunteers) will test the efficacy of our game to elicit VOR motor learning in 18 healthy volunteers with no history of vestibular disease. Each subject will play the game

twice for sessions of 300 trials each (about 30 minutes of game playing). In one of these sessions, the game will be structured to increase VOR gain in a single step and in the other session, the gain increase will be advanced incrementally to the same final target. The hypothesis predicts that the latter paradigm will lead to more efficient learning. The specific procedures for Aim 1 will be as follows:

Each subject will participate in two separate sessions on different days. In one session, the full visual-vestibular mismatch (x1.5) will be introduced at the start of the game (paradigm A) and in the other session scene motion will be gradually adjusted to adapt the VOR incrementally (paradigm B). Each session will consist of 300 trials. To eliminate an order effect, the paradigm order will be randomized across the group of subjects: half will do paradigm A first, and the other half will begin with paradigm B.

Aim 2 (Vestibular Patients) will test the playing experience of 12 subjects with peripheral vestibular disorders and will obtain preliminary data regarding efficacy and feasibility of the game for clinical vestibular therapy. The experimental protocol will be similar to that of Aim 1 (see above), with recording of both eye and head positions during VOR testing and game playing. The active and passive VOR, as well as DVA, will be recorded before and after the game. For each subject, we will begin by determining the baseline VOR gain. The game will then be played with a scene motion that corresponds to a VOR gain that is 20% higher than the baseline value for active rotation, separately set for each direction of head rotation. For example, if a patient with left vestibular hypofunction has a baseline VOR gain of 0.5 for active turns to the left, then scene motion will be set to x0.6 viewing (20% higher than 0.5). The subject will play the entire game with this condition, rather than advancing the difficulty as in Aim 1, because in clinical rehabilitation the difficulty is advanced more slowly, in a series of sessions over weeks of therapy.

Data Acquisition: We will record head position using our 3-D magnetic-field coil system, long considered the gold standard for measuring eye and head rotations, due to its accuracy and high signal-to-noise ratio. Our system has large field coils (6 ft cube), which provides an adequate area of homogeneity at the center of the field for head-free recordings. Eye movements will be recorded simultaneously using a lightweight head-mounted video-oculography (VOG) system (IScan) that records 2-D eye position at 240 Hz. Analog VOG pupil-tracking data are saved together with the head coil signals in the same file for reliable synchronization of eye and head. Finally, calibrated head positions will be calculated in real time (via Simulink Real Time) and sent over UDP to the gaming computer to drive scene motion at the specified visual-vestibular mismatch. A computer-generated log file will record data from each trial: instructed direction of head movement; optotype size, orientation, and on-time; the subject's key-press response; and a time-stamp for synchronization with the recorded head and eye position data.

Data Analysis: Data are analyzed using custom programs that are written by the PI and study staff. In some cases. electronic data from head and eye movement recordings will be transported offsite for data analysis using specialized software. The data files to be analyzed will be coded so that they can be reconnected with the correct subject when the data are returned to the LSCDVAMC, but they will not contain other subject identifiers. The code will be stored only at the LSCDVAMC (as per Q56), so there will not be a way to connect data to a specific subject when the data are offsite.

14. Will the research involve the following?

☐ **N/A** **Chart/Data Review**

Placebo Group	☒ **No**	☐ **Yes** *(describe)***:**
Other Control Group	☒ **No**	☐ **Yes** *(describe)***:** Note that although healthy individuals without vestibular disease will participate in the study, they will be the subjects of Aim 1, not controls for the vestibular patients of Aim 2 (the two Aims have different objectives).
Randomization	☐ **No**	☒ **Yes** *(describe)***:** The only randomization will be the order of the two playing sessions in Aim 1.
Deception	☒ **No**	☐ **Yes** *(describe)***:**

15. Does the research involve the use and/or disclosure of Individually Identifiable Health Information in any form or medium?

☐ **No** ☒ **Yes** **If yes, complete the required HIPAA Waiver/Authorization forms.**

16. Does the study include the administration of a study agent that does not require FDA approval and does not require an IND (e.g. vitamins, food supplements, isotope tracers, alternative medicines, etc.)?

☒ **No** ☐ **Yes -***provide a detailed description of the procedures used to assure patient safety:*

17. Will radioactive material be administered or will subjects be exposed to ionizing radiation?

- *Ex. Radiographic equipment, fluoroscopic equipment, and CT scanners, etc.*

☒ **No** ☐ **Yes**

18. In your judgment, could the objectives of the research be met in a way that presents less risk to subjects?

☒ **No** ☐ **Yes** *please explain***:**

Section 4 – Subject Selection, Recruitment, and Vulnerable Populations

19. Anticipated duration of entire study reported in years: The study as proposed is expected to last for 6 years (a one-year extension was approved by VA RRD, an additional no-cost extension will be requested to complete enrollment and study procedures, follow-on years for additional data analysis, including preparation of the next funding proposal).

20. Estimated number of subjects to be studied at the LSCDVAMC or charts/records to be reviewed.

- *Provide answers for **each cohort** including normal controls; (patients, family members, treating physicians,)***:**

AIM 1: Healthy volunteers: 30 (per the funded protocol, enrollment will be stopped when completed data are obtained for 18 subjects)
AIM 2: Vestibular Patients: 20: (per the funded protocol, enrollment will be stopped when completed data are obtained for 6 subjects with unilateral hypofunction and 6 subjects with bilateral hypofunction)

Note that it may be necessary to enroll more than the targeted number of subjects in order to reach the goals, if some subjects drop out before completing the full study.

21. Estimated number of subjects to be studied or charts/records to be reviewed at all sites

- *Provide answers for **each cohort** including normal controls; (patients, family members, treating physicians,)*

N/A SINGLE SITE ☒

22. Duration of individual subject participation

*Provide answers for **each cohort** including normal controls; (patients, family members, treating physicians,).* Each experimental session is expected to last approximately one hour. Healthy volunteers who are the subjects of Aim 1 will each participate for two recording sessions. Vestibular patients who are the subjects of Aim 2 will each participate for four sessions. Analysis of subjects' data will continue for the duration of the study.

Chart/record review ☐ **N/A**

23. Age range of subjects

- *provide answers for **each cohort**, including normal controls*:

☐ **Adults 18 years or greater**

☒ **Specific age range** (list age range): 18-75

☐ **Children –waiver from VACO:** ☐ **attached** ☐ **pending- *provide submission date:***

***Contact AO/Research holly.henry@va.gov for guidance..*

24. Which of the following will be recruited or reviewed for this study *(check all that apply)*?

☐ **Veteran Inpatients**
☒ **Veteran Outpatients**
☐ **Veteran Families**
☒ ***Normal volunteers**
☒ **Men**
☒ **Women**

☒ ***Non-Veterans; Provide justification** For Aim 1, there may be few healthy veterans available who are eligible and willing to participate.

*According to VHA Handbook 1605.04 Notice of Privacy Practices VHA must provide a copy of its VHA Notice of Privacy Practices to all non-Veteran patients (e.g., active duty personnel or those seeking care in humanitarian circumstances) receiving care or treatment at a VHA health care facility or non-Veteran research subjects enrolled in an approved VHA research study with clinical trials. VA Form 10-0483 Acknowledgement of the Notice of Privacy Practices should be signed by the non-Veteran research subject at the time of consent and given a copy of the Notice of Privacy Practices. Once the Acknowledgement Form is signed please send a copy to the Privacy Officer. If additional information is needed please contact your Facility Privacy Officers Joseph Picklo or Tomica Jefferson joseph.picklo@va.gov / phone 8214102 tomica.jefferson@va.gov / phone 8214101.

25. Which vulnerable population(s) will be TARGETED for recruitment in this study:

- *Indicate only those populations that are specifically targeted for the research described in this document.*
- ***It is not necessary to check any box if, for example, your study will include a full range of subjects, some of whom may be elderly or subjects who might incidentally be employees.***

☐ **N/A Chart Review** (*proceed to Item 30*)

☒ **NONE (***proceed to Item 26)*

☐ **Medical students, house staff, or Employees of the VAMC or Case**

☐ **Pregnant Women OR Women who are Breastfeeding, Human Fetuses, or Neonates**

☐ **Children – Complete Section 14 "Children as Research Subjects"**

☐ **Prisoners (The LSCDVAMC does not conduct research involving prisoners)**

☐ **Targeting Persons over Age 65**

☐ **Persons with Acute/Severe Mental/Physical Disabilities** *(describe)***:**

☐ **Persons with Cognitive, Social, Economic, or Educational Disadvantages** *(describe)***:**

☐ **Others** *(describe)***:**

a. Provide the Scientific and Ethical reasons for Targeting these vulnerable populations in the research:

b. What additional safeguards or provisions will be used to protect the rights and welfare of the identified targeted vulnerable subjects?

☐ **Surrogate consent**

☐ **Subject assent**

☐ **Use of a consent or Medical monitor**

☐ **Use of a waiting period**

☐ **A patient advocate will participate in the informed consent process**

☐ **Key elements of informed consent will be presented orally**

☐ **No supervisor or rater will be involved in obtaining consent**

☐ **Other - Describe Additional safeguards you plan to use:**

c. Describe the procedures used to ensure that the subject's legally authorized representative is well informed regarding his/her role and obligation to protect persons with impaired decision making capacity:

26. Procedures for Recruiting Subjects -check all that apply and attach all recruitment materials:

☐ **Not Applicable**

☒ **Materials**; **Recruitment Letter, Posting on Bulletin Board, Brochure, Flyer, Post card, etc.**

☐ **Media; Internet Ads, Press Releases, Newspaper, Radio**

☒ **Investigator's Patient Population**

☒ **Physician Referral**

☐ **Letters to Physicians/Clinicians**

☒ **Other** *(describe)***:** Referrals from physical therapy, audiology; CPRS chart review (see #27 below)

27. Will VA computer systems be used to identify potential subjects?

- *e.g. VISTA, CPRS, Pharmacy Databases, other clinical databases, etc,*

☐ No ☒ Yes- Describe how the computer will be used to identify patients. List all systems used and all information to be collected: Potential subjects for Aim 2 (patients with vestibular hypofunction) will be recruited from the population of patients in the VANEOHS clinics that treat vestibular disorders. In addition to direct referrals, the P.I. will review the medical records of patients that have been seen in these clinics (CLE NEURO VESTIBULAR WALKER, CLE NEURO VESTIBULAR STAHL, CLE ENT clinics, CLE AUDIOLOGY BALANCE, CLE PT VESTIBULAR BALANCE) to identify veterans who may be eligible to participate. These veterans will be sent a recruitment letter describing the study and offering them the opportunity to be considered for participation. A number will be provided for the veteran to call to express interest or to decline to participate. It will also explain that if no response is received within 2 weeks from the mailing of the letter, the veteran may receive a follow-up call by study staff.
In some cases, even for patients recruited by direct referral, it may be necessary for the PI to review a potential subject's medical record in CPRS to confirm eligibility, before the subject is consented and enrolled in the study. Identifiers that will potentially be accessed include: Name, Date of Birth, Social Security Number, Medical History, Imaging

28. Will subjects be identified and/or recruited in clinics and/or inpatient wards at the LSDCVAMC?

☐ No ☒ Yes- **explicitly describe your process for identifying and/or recruiting these patients:** *(address all cohorts):* Patients will be recruited by Dr. Walker from the VANEOHS neurology clinic or will be referred by other providers. As above, patients will also be identified by review of CPRS records of patients seen in those clinics.

29. In addition to the consent form will any other materials be given to the subject?

☐ **N/A Chart/data review**

☐ **No** ☒ **Yes- check all that apply and submit for IRB review:**

☐ **Letter**

☐ **Information Sheets**

☒ **Questionnaire, Survey, Diary**

☒ **Other** *(flyer, brochure, describe):* The recruitment flyer and recruitment letter with study information will be used to advertise the study to potential subjects.

30. Please list by bullet point inclusion/exclusion criteria for the study.

- *Entry criteria should be as detailed as necessary to define the subject population(s) under study and reduce confounding design. Include precise criteria for age, gender, and other relevant factors.*

- *List specific exclusion criteria which could interfere with the study design or place a subject at risk during the study.*

- *Provide answers for **each cohort**, including normal controls.*

AIM 1: Healthy Volunteers

- Adults age 18-75
- No history of vestibular disease
- Equivalent visual acuity at testing distance of 20/30 or better without or with spectacles

AIM 2: Vestibular Patients

- Adults age 18-75
- Peripheral vestibular hypofunction (unilateral n=6, bilateral n=6)
- No central vestibular disorder
- Equivalent visual acuity at testing distance of 20/30 or better without or with spectacles

☐ **N/A Chart/data review**

31. By role, (PI, Coordinator, etc.) who will assess for eligibility and how will this be accomplished?

The PI will assess all potential subjects for eligibility by personal interview and a brief clinical examination. Veterans who are potential subjects for Aim 2 will be further assessed for eligibility by a review of their medical record pertaining to the diagnosis of peripheral vestibular disease.

32. Are any subjects excluded on the basis of race, ethnic group, understanding of English, socioeconomic status, education, gender, or pregnancy?

- *Note: It is appropriate to indicate that you do not anticipate encountering potential subjects who do not speak English **based on the population to be studied***

☐ **No** ☒ **Yes -** *(provide justification)***:** All subjects will need to understand English sufficiently to follow instructions during the experimental session.

☐ **N/A Chart/data review**

33. Will subjects be reimbursed or paid an incentive for participating?

☐ **No (skip to item #35)** ☒ **Yes**

☐ **N/A Chart/data review (skip to item #38)**

34. How and when will they be paid?

☐ **Cash** ☐ **Check** ☒ **Other** -please explain**:** They will receive a voucher from the PI that they will take to the Agent Cashier to be paid.

☒ **Prorated** -provide schedule**:** $30 for each session completed ☐ **Fixed** -provide schedule

35. Will subjects be responsible for any of the costs related to the research?

☒ **No** ☐ **Yes-** please explain**:**

36. Will treating physicians, clinicians, or researchers be compensated or paid an incentive for referring or enrolling subjects?

☒ **No** ☐ **Yes** -please explain**:**

37. Please describe steps you will take to ensure that subject selection is fair and equitable:

We will accept all adult subjects regardless of gender or ethnicity, who are interested and eligible for the study.

Section 5 – Risks and Benefits

38. Please list by bullet and describe the reasonably foreseeable physical, psychological, social, economic, and privacy risks, side effects, or discomforts associated with the research and their expected frequency and severity.

- *If this study is a retrospective chart review, or involves only the analysis of data, risk may still be present in the form of data security concerns.*

• There may be mild motion sickness or disorientation when the subject's head is turned or from the visual motion on the screen.

• Research data could be inadvertently disclosed.

*Certificate of Confidentiality:

- Certificates of Confidentiality are issued by the National Institutes of Health (NIH) to protect identifiable research information from forced disclosure.
- They allow the investigator and others who have access to research records to refuse to disclose identifying information on research subjects in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level.
- Certificates of Confidentiality may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation.
- By protecting researchers and institutions from being compelled to disclose information that would identify research subjects, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by assuring confidentiality and privacy to subjects.
- **For more information, see http://grants1.nih.gov/grants/policy/coc/index.htm.**

39. Is this project principally concerned with the collection of sensitive information such as sexual attitudes, use of drugs or addictive products, and illegal conduct that would need to be protected against subpoena or forced disclosure in order to protect subjects?

☒ No

☐ Yes- will an application for a *Certificate of Confidentiality be submitted to the National Institute of Health upon IRB approval (or approval contingent on the issuance of such a certificate)?

☐ Yes ☐ **No provide a justification as to why a Certificate of Confidentiality will not be obtained:**

40. Describe all procedures that minimize risks, please include study and standard of care procedures:

• If the subject becomes too motion sick, he/she may stop the experiment at any time. Both the head movements and the visual stimulation that are a part of this study are comparable to what is experienced in everyday life and in routine clinical examinations.

• Research data will be secured in several ways. First, all paper forms, including consent forms, will be kept in a locked cabinet in the PI's locked office, within the Daroff-Dell'Osso Ocular Motility Laboratory. Second, electronic data will be stored on encrypted drives (non-networked encrypted drive in the Daroff-Dell'Osso Ocular Motility Laboratory and encrypted VA networked drive [Ocular Motility Research Drive]). Moreover, the only identifiers associated with these binary data files are the subject code and the timestamp indicating when the files were created and the data was collected. No more explicit subject indentifiers, such as name, birthdate, SSN, or any clinical diagnosis information, are contained in these coded files.

41. Describe alternative procedures or course of treatment, if any, which might be advantageous to the subject. State if no alternatives exist or if this is not a treatment study.

This is not a treatment study.

Minimal Risk: Minimal risk means that the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

42. Please give your overall risk classification for the research:

☒ **Minimal Risk**

☐ **Greater than Minimal Risk**

43. Will subjects receive any <u>direct</u> benefit from this research?

☒ **No** ☐ **Yes** -describe the direct benefits**:**

44. Please explain briefly why you consider the risks associated with the study to be reasonable in relation to its benefits?

The risk is minimal and is comparable to that experienced in normal everyday life and in clinical examinations. This risk is small compared to the potential long-term benefit of more effective treatment for these functionally disabling disorders.

Section 6 – Informed Consent

45. Type and number of Consent-

- *When more than one consent form is being used a descriptor MUST be in the header section describing the population and/or phase of the study***:**

☒ **Written Informed Consent –number used in this study** 1

☐ ***Oral Script/Letter/Information Sheet- number used in this study *Submit Request for Consent Waiver Form-waiver of documentation of informed consent**

☐ **No informed consent at all in this study- Submit a Request for Consent Waiver Form-waiver of informed consent and proceed to item 53**

46. Will all adult subjects have the capacity to give informed consent?

☒ **Yes** ☐ **No- Describe range of impairment.**

- *Research involving more than minimal risk, capacity should be determined by a psychiatrist, clinical psychologist, or other qualified professional not otherwise involved in the research.*
- *Individuals who lack the capacity to consent may participate in research only if a legally authorized representative gives consent on their behalf.*

n/a

47. Will anyone other than the subject be authorized to provide consent or permission for the subject's involvement in the research?

- *e.g., parents, court ordered guardian, spouse, etc.*

☒ **No** ☐ **Yes -**please explain**:**

48. Describe <u>how</u> and <u>where</u> informed consent will be obtained:

If a potential subject calls to inquire about the study, the details of the experiment will be explained, and he or she will be offered a consent form to review at home, if desired. The actual consent process will take place in the Daroff-Dell'Osso Ocular Motility Laboratory when a potential subject comes for the experiment. At that time, the study will again be explained in detail by the PI or co-I, the potential subject's understanding of the procedure will be confirmed, and the subject will be given the opportunity to sign the consent form or to decline to participate.

49. Will there be an opportunity for potential subject to take the consent form home to discuss participation and options with family members?

☒ **Yes** ☐ **No -** please explain**:**

50. List by role who will be obtaining informed consent from subjects or their legally authorized representatives:

- *ex. study coordinator, co-investigator, research nurse***,** *research assistant, PI*

PI, co-investigator

51. Please describe how informed consent will be obtained from subjects who do not read or understand English;

- *identify any languages likely to be encountered, and attach a copy of a translated and authenticated informed consent document*

- *It is appropriate to indicate that you do not anticipate encountering potential subjects who do not speak English based on the population to be studied*

  We do not plan to enroll subjects who do not understand English. It is necessary that all subjects understand English, so that will be able to follow the instructions during testing sessions.

52. Describe who *(by Role ex. PI, Coordinator, etc.)* **and how it will be determined that subjects and/or legally authorized representative understand the research and their rights.**

- *ex. question and answer, repeat back parts of the research, describe a procedure…etc*

The PI or co-investigator will confirm understanding by asking potential subjects to repeat back the expectations and potential risks.

Section 7 – Privacy and Confidentiality

Privacy - refers to a person's desire to control the access of others to themselves. For example, persons may not want to be seen entering a place that might stigmatize them, such as a pregnancy counseling center that is clearly identified as such by signs on the front of the building. Privacy concerns people, whereas confidentiality concerns data. The research proposal should outline strategies to protect privacy including how the investigator will access information about potential subjects.

In developing strategies for the protection of subjects' privacy, consideration should be given to:

- Methods used to identify and contact potential subjects
- Settings in which an individual will be interacting with an investigator
- Appropriateness of all personnel present for research activities
- Methods used to obtain information about subjects and the nature of the requested information
- Information that is obtained about individuals other than the "target subjects," and whether such individuals meet the regulatory definition of "human subject" (e.g., a subject provides information about a family member for a survey)
- How to access the minimum amount of information necessary to complete the study

Confidentiality - methods used to ensure that information obtained by researchers about their subjects is not improperly divulged. Confidentiality refers to the researcher's agreement with the subject about how the subject's identifiable private information will be handled, managed, and disseminated. The research proposal should outline strategies to maintain confidentiality of identifiable data, including controls on storage, handling, and sharing of data. When appropriate, certificates of confidentiality could be used to maintain the confidentiality of identifiable data

When the IRB evaluates research proposals for strategies for maintaining confidentiality, where appropriate, consideration will be given as to whether:

- Methods to shield subjects' identity adequately protect subject privacy
- There is a long-range plan for protecting the confidentiality of research data, including a schedule for destruction of identifiers associated with the data
- The consent form and other information presented to potential research subjects adequately and clearly describe confidentiality risks.
- The informed consent process and the informed consent document, and if applicable the Authorization Form, clearly delineates who will have access to the subject's information and under what circumstances data may be shared (i.e., government agencies, sponsors).

53. Describe when and where subjects will provide their information. Include the nature of the information and who will receive and use the information. Document the provisions used to protect privacy interests of those subjects when gathering their information and data.

For subjects with vestibular disorders (Aim 2), basic clinical information will most often have been obtained at the time of clinical evaluation or may be provided by the referring medical provider. Additional information, such as completion of questionnaires, will be obtained in the private conference room of the Daroff Dell'Osso Ocular Motility Laboratory. The information collected will include the neurological history, vestibular symptoms reported, the clinical neurological examination, and the symptom questionnaires. This information will be important for interpreting the results of the study. The primary data for experiments in this study will be in electronic form and will consist of recordings of eye movements and game playing. Data will be secured, and only research study staff will have access to them. Results will be shared and published publicly only in de-identified form.

54. Will researchers have access to identifiable private information about potential subjects <u>outside</u> of this research project? *Ex. PI is provider who has access to medical records for clinical care*

☐ **No** ☒ **Yes- please explain:** The PI is a VA staff physician who has access to medical records as part of patient care.

55. Will Researchers collect identifiable private information on anyone other than the subject?

- *Ex. family members, friends, colleagues, classmates…etc.*

☒ **No** ☐ **Yes -please explain:**

56. At the time data are transcribed or recorded for this study they are?

☐ **Fully identifiable- list identifiers to be collected:**

☒ **Coded with a unique identifier- describe the code:** sequential code

a. Who will have access to the key? The PI

b. Where is the key maintained? Two locking barriers must be in place between the coded data and the key. A paper copy of the key will be kept in a locked file cabinet in the PIs locked office. An electronic version will be kept on the PI's encrypted VA network drive

☐ **De-identified-by Privacy Officer or Statistician.**

☐ **Other** *(describe)***:**

57. How will electronic research data be secured while the study is active?

☐ **No electronic data will be stored**

☐ **VA encrypted laptop**

☒ **Encrypted VA device/media- describe:** stored on encrypted drive in Ocular Motility Laboratory (BC300F) with password protection

☒ **VA network drive;**

☐ **M: drive; whose?**

☐ **S: drive**

☐ **Folder access password protected**

☒ **Other drive location** *(for example P: drive)*: Ocular_motility on \\vhaclehsm01\Research

☐ **Folder access password protected**

58. How will hardcopy research data be secured while the study is active? Two locking barriers must be in place.

☐ **No hardcopy data will be stored**

☒ **Locked office and locked file cabinet**

☐ **Data coded by PI or study staff with a master list secured and kept separately**

☐ **Data de-identified by Privacy Officer or Statistician- *(*VA does not consider coded data to be de-identified)**

☐ **Other -specify:**

59. Provide the physical location including room number (and address if outside of this VA) where all electronic and hardcopy data will be stored: Wade Park: BC300R, BC300F, BE 215.

60. Is identifiable information physically or electronically sent <u>TO</u> the LSCDVAMC from other institutions or locations?

☒ **No** ☐ **Yes -** contact Privacy Officer Joseph Picklo or Tomica Jefferson joseph.picklo@va.gov / phone 8214102 tomica.jefferson@va.gov / 8214101 or Information Security Officer Bruce Frankford bruce.frankford@va.gov / phone 821 1604 – prior to submitting to the Research Service**.**

****If yes complete the following:**

a. LSCDVAMC investigator will receive:

☐ **Hardcopy information or specimens**

☐ **Electronic information**

b. What are the procedures for transporting and/or transmitting identifiable information securely?

c. What will be the final disposition of the identifiable data transferred to the LSCDVAMC?

Records will be retained in accordance with RCS 10-1.

61. Is identifiable information physically or electronically sent <u>FROM</u> the LSCDVAMC to other institutions or locations?

☒ **No** ☐ **Yes** contact Privacy Officer Joseph Picklo or Tomica Jefferson joseph.picklo@va.gov / phone 8214102 tomica.jefferson@va.gov / 8214101 or Information Security Officer Bruce Frankford bruce.frankford@va.gov / phone 821 1604 – prior to submitting to the Research Service

****If yes complete the following:**

a. The LSCDVAMC investigator will send:

☐ **Hardcopy information or specimens**

☐ **Electronic information**

b. What are the procedures for transporting and/or transmitting identifiable information securely?

c. What will be the final disposition of the identifiable data transferred offsite?

Records will be retained in accordance with RCS 10-1.

Files containing the results of the data analysis will be returned to the LSCDVAMC and stored electronically along with the original data files from the same subject, as per Q57.

62. Record Control Schedule 10-1 indicates all research records must be retained indefinitely. Please indicate where this information will be stored and the safe guards to protect it:

a. Electronic Safeguards:

☐ **No electronic data will be stored**

☐ **VA encrypted laptop**

☒ **Encrypted VA device/media- describe:** stored on encrypted drive in Ocular Motility Laboratory (BC300F) with password protection

☐ **VA network drive;**

☐ **M: drive; whose?**

☐ **S: drive**

☐ **Folder access password protected**

☒ **Other drive location** *(for example P: drive)***:** Ocular_motility on \\vhaclehsm01\Research

☐ **Folder access password protected**

b. Hardcopy safeguards. Two locking barriers must be in place.

☐ **No hardcopy data will be stored**

☒ **Locked Office and Locked File Cabinet**

☐ **Coded by Study Staff**

☐ **De-identified by Privacy Officer or Statistician**

☐ **Other- Describe:**

Facility name, address, and room number where hardcopy or electronic data will be stored:

Section 8 – Data and Safety Monitoring –Greater than Minimal Risk Study

- For all research that is greater than minimal risk a Data and Safety Monitoring Plan must be developed.

- This is a plan to assure the research includes a system of appropriate oversight and monitoring of the conduct of the study to ensure the safety of subjects and the validity and integrity of the data.

***CHECK BOX IF THIS IS A MINIMAL RISK STUDY ☒ SKIP TO #65**

63. Safety monitoring for this greater than minimal risk project will include:

☐ **Data Safety Monitoring Board**:

☐ **Data Monitoring Committee**

☐ **Other**

- *Attach the plan or provide details including whether committee is independent from the study sponsor, how often it meets, whether written reports are available, etc*

64. Describe the plan for on-site data monitoring by the sponsor, contract research organization (CRO), or other independent body:

- **Research Office must be notified of all on-site monitoring visits.*

65. Conditions that may result in removal of subjects from the research *(check all that apply)*:

☐ **Medical condition unchanged**	☐ **Medical condition worsened**
☒ **Serious adverse event**	☐ **Intolerable complications**
☐ **Pregnancy**	☒ **Investigator's clinical judgment**
☒ **Subject withdrawal**	☒ **Subject uncooperative or noncompliant**
☐ **Study closure by sponsor or FDA**	☐ **Refusal to suspend breast-feeding**
☐ **Other-describe:**	☐ **Not Applicable**

66. If a subject withdraws or is removed from the study, describe the potential risks of early withdrawal and the procedures in place to minimize these risks:

Section 9 – FDA-Regulated Drugs/Biologics

NOTE: If this research involves the use of <u>any</u> drugs or biologics, the study is subject to the Food and Drug Administration (FDA) regulations.

- **Documentation of FDA approval for the experimental use of these agents must be provided for review (industry sponsored protocol listing the IND number, letter from the FDA, letter from industry sponsor, or other document and/or communication verifying the IND for this study).**
- All drug/biologic products must be dispensed and tracked through the LSCDVAMC Research Pharmacy.
- An M.D. must be part of the Research Team for all studies that involve the use of a device or drugs.
- The LSCDVAMC Pharmacy and Therapeutics (P&T) Committee must approve: (1) Studies of investigational drugs (2) research involving an FDA-approved drug used in a non-approved manner, and (3) an FDA-approved drug, used as approved, when its use is part of a research protocol.

- **VA Form 10-9012 Investigational Drug Information Record** –must be completed for each drug being evaluated in a research study, regardless of IND status. In addition, the VA Form 10-9012 provides a listing of all authorized prescribers for the study drug(s).

67. Type of Product- check all that apply:

☒ **Not Applicable -No FDA-regulated drugs/biologics involved – Proceed to Section 10**

☐ **Drug**

☐ **Biologic or Other:**

68. Type of Trial *(check as applicable)***:**

☐ **Phase I** ☐ **Phase II** ☐ **Phase III** ☐ **Phase IV** ☐ **NA**

Phase I Trials: Initial studies to determine the metabolism and pharmacologic actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness; may include healthy subjects and/or patients.
Phase II Trials: Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks.
Phase III Trials: Expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide adequate basis for physician labeling.
Phase IV Trials: Post-marketing studies to delineate additional information including the drug's risks, benefits, and optimal use.

69. FDA Status of Drugs/Biologics –

*** For drugs, an IND may not be necessary if ALL seven of the following conditions are met:**

1. The drug being used in the research is lawfully marketed in the United States;
2. The research is not intended to be reported to FDA in support of a new indication for use or to support any other significant change in the labeling for the drug;
3. The research is not intended to support a significant change in the advertising for the product;
4. The research does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
5. The research is conducted in compliance with the requirements for IRB review and informed consent (21 CFR parts 56 and 50, respectively);
6. The research is conducted in compliance with the requirements concerning the promotion and sale of drugs (21 CFR 312.7);
7. The research does not intend to invoke 21 CFR 50.24 (Exception from informed consent requirements for emergency research).

Provide the following information for <u>each</u> drug/biologic used in this study:

Trade and Generic Name	**Manufacturer**	FDA Approved	**Product use consistent with product labeling**	**IND Required***	**IND Number**	**IND Sponsor or Holder****

70. **When the PI holds the IND, complete the following:

i. The PI has reviewed the Guidance on Requirements of the Sponsor and the Investigator as Sponsor

☐ **Yes**

ii. As the PI, you will comply with the regulatory responsibilities of a sponsor

☐ **Yes**

71. Drug Information for each drug listed in the protocol -check as applicable

☐ **Approved Drugs**

☐ **Not Approved**

- **Attach VA Form 10-9012 Investigational Drug Information Record for each drug used in the protocol**
- **Attach Package Insert or PDR monograph – copy ready, 8.5 x 11 for each drug listed in the protocol**
- **Attach Investigator's Brochure**

72. Provide a detailed description of how FDA-regulated drugs/biologics will be stored, secured, dispensed, administered, tracked, and returned.

Section 10 – FDA-Regulated Devices

This section should be completed for a medical device that is the <u>subject</u> of a clinical study designed to evaluate the effectiveness and/or safety of the device.

- An investigational device may be an FDA approved device that is being studied for an unapproved use or efficacy. This also includes an approved device that is being studied for an unapproved or approved use in a controlled, randomized, or blinded clinical trial.
- Documentation of FDA approval for the experimental use of the device must be provided for review (industry sponsored protocol listing the IDE number, letter from the FDA, letter from industry sponsor, or other document and/or communication verifying the IDE for this study).

Device Risk Determination:

Significant Risk (SR) Device is an investigational device that: (1) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject, or (2) is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; or (3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Non significant Risk (NSR) Device is a device other than a significant risk device.

The IRB is required to document the basis for risk determination based on the proposed use of a device in the research by considering the nature of the harm that may result from the use of the device. FDA has the ultimate decision in determining SR and NSR.

An M.D. must be part of the Research Team for all studies that involve the use of a device.

The Environment of Care Committee (EOC) must approve all research that involves electrically line-operated devices, which have leads or electrodes and will come in contact with human subjects.

73. Type of Product-check all that apply:

☒ **Not Applicable -No FDA-regulated devices involved – Proceed to Section 11)**

☐ **An FDA regulated device will be used BUT not with intent of studying safety or efficacy (***Proceed to Section 11)*

☐ **Device**

74. List the device-include name and manufacturer:

75. FDA Regulatory Status of the Device:

☐ **FDA Approved Device**

- **A device approved by the FDA for distribution, marketing, sale to, and use by, the public for the study's indication.**

☐ **New Indication of an FDA Approved Device**

- **A device NOT approved by the FDA for distribution, marketing, sale to, and use by, the public for the indication used in the study.**

☐ **Investigational - Investigational Device Exemption (IDE)**

- **An FDA designation that permits a manufacturer to lawfully ship an unapproved device for use in a research study.**

Provide the following:

a. IDE Number:

b. IDE Sponsor or Holder:

If the PI holds the IDE, complete the following:

i. The PI reviewed the Guidance on Requirements of the Sponsor and the Investigator as Sponsor

☐ **Yes**

ii. As the PI, you will comply with the regulatory responsibilities of a sponsor

☐ **Yes**

c. FDA or Sponsor Device Risk Determination

☐ **Non-Significant Risk**

☐ **Significant Risk**

d. Attach documentation of FDA approval for the experimental use of the device (industry sponsored protocol listing the IDE number, letter from the FDA, letter from industry sponsor, or other document and/or communication verifying the IDE for this study).

☐ **Humanitarian Use Device (HUD)**

- **An FDA designation for a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer**

than 4,000 individuals in the United States per year. For more information about Humanitarian Use Devices see the HRPP SOP manual on the R&D website.

Provide the following:

a. HUD Number:

b. HUD Sponsor or Holder:

c. Include a copy of the FDA letter granting Humanitarian Use Device (HUD) status.

☐ **510(k) Status –**

- **A device determined by the FDA to be "substantially equivalent" to an existing device that is legally marketed in the U.S. Until a 510(k) device is approved, it is still considered investigational.**

a. Provide the name of an equivalent device and sufficient documentation to justify 510(k)

76. Attach device information (i.e., brochure, device label)

77. Provide a detailed description of how FDA-regulated devices will be stored, secured, dispensed, administered, tracked, and returned.

Section 11 – Genetic Testing and Discovery of Genetic Information (DNA)

78. Does the research involve genetic testing or DNA/RNA extraction?

☒ **No genetic testing (***Proceed to Section 12)*

☐ **Yes- complete the following:**

a. Describe the purpose of the genetic testing component of the study

- *Is it to establish risks, associations, or prevalence?*

b. Describe whether the test is a standard test already in clinical use or a new or experimental laboratory study

c. Describe the accuracy of the test

- *Sensitivity, specificity, reliability, validity, and variability*

79. Does an abnormal test result indicate that the subject:

☐ **Has a specific condition**

☐ **Is at risk for a specific condition**

☐ **May be at risk for a specific condition**

☐ **Has, is, or may be at risk for some other outcome**

☐ **Other** *(describe):*

80. Does a normal test result indicate that the subject

☐ **Is not at risk for a specific condition**

☐ **Is at a lower risk for a specific condition**

☐ **Is at a population risk for a specific condition**

81. Is there a risk of discovery of other results such as non-parentage or other genetic conditions?

☐ **No** ☐ **Yes- please explain:**

82. Will test results produce information on anyone (e.g. a first-degree relative) besides the subject?

☐ **No** ☐ **Yes- please explain:**

83. To whom and in what manner will genetic information be reported?

84. Will genetic counseling be made available to subjects?

☐ **No** ☐ **Yes- indicate who will conduct the counseling and whether there are any additional charges:**

85. Will DNA samples be stored?

☐ **No** ☐ **Yes--describe where, how, and for how long the samples will be stored:**

86. Who will own the DNA samples?

87. Will there be any subsequent analysis of the DNA samples?

☐ **No** ☐ **Yes- describe the purpose of the subsequent analysis and whether there will be dissemination of any new information:**

88. Describe how samples will be handled if the subject withdraws consent for further participation:

89. Will the samples be distributed to other investigators?

☐ **No** ☐ **Yes- please explain:**

90. Describe the provisions to maintain the confidentiality of research data, especially in cases where data can be linked to individual subjects:

Section 12 – Tissue Collection/Storage/Banking*

It is VA policy to ensure that human biological specimens, as well as the linked data collected as part of research projects conducted by VA investigators in VA facilities or approved off-site locations, are maintained at *VA approved tissue banks or VA-sponsored tissue banks.

See VHA Directive 2000-043 "Banking of Human Research Subjects' Specimens" for more information and also visit http://www.research.va.gov/programs/tissue_banking/default.cfm

Human biological specimens (specimens).

- **Human biological specimens are materials, such as blood, urine, tissue, organs, hair, nail clippings, buccal swabs or any other materials that are derived from human subjects and are either collected specifically for research purposes or as residual specimens from diagnostic, therapeutic or surgical procedures.**

91. *Does the research involve storage or banking of human specimens or identifiable private information for use in future studies? *(check all that apply)*

☒ **No** *(proceed to Section 13)* ☐ **Yes-describe status of VA approved or VA sponsored facility:**

☐ **Storing or banking identifiable private information**

☐ **Storing or banking human specimens**

Please provide the following information:

a. What identifying information will be required?

b. What are the foreseeable uses of the specimens (e.g., research, pharmaceutical products, production of cellular lines for various uses, etc.)?

c. What is the VA approved or VA sponsored location/institution where the information and/or specimens will be stored?

d. How long will the information and/or specimens be stored?

e. Is the storage facility an on-site or off-site location?

f. Will subjects be able to request that their specimen and/or information be withdrawn from the bank or repository? *(explain)*

Section 13 – Children as Research Subjects

Research involving children must not be conducted by VA investigators while on official duty or at VA or VA-approved offsite facilities unless a waiver has been granted by the CRADO (See VHA Directive 2001-028 "Research Involving Children" for more information.

92. Do you plan to enroll children as research subjects?

☒ **No** *(Proceed to Section 14)*

☐ **Yes- Age range of subjects:**

93. Category of Research *(Check the box next to the category of research you believe your research falls under. The IRB will make a final category determination during review.)***:**

☐ **Research involving minimal risk (the probability & magnitude of harm or discomfort anticipated are not greater than those ordinarily encountered in daily life or during routine physical or psychological tests.)** *(46.404)*

☐ **Research involving greater than minimal risk but of potentially direct benefit to the subject.** *(46.405)*

☐ **Research involving greater than minimal risk and no prospect of direct benefit to the subject but likely to yield generalizable knowledge about the subject's disorder or condition.** *(46.406)*

☐ **Research not otherwise approvable which presents an opportunity to understand, prevent or alleviate a serious problem affecting children/decisionally impaired adults.** *(46.407)*

94. Do you anticipate enrolling minors who are wards of the state?

☐ **No** ☐ **Yes**

95. Permission of parents or guardian *(check one only)***:**

☐ **The permission of each child's parents or guardian will be sought unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child (required for categories 46.406 and 46.407 above in item 104).**

☐ **The permission of only one parent will be sought (acceptable for categories 46.404 or 46.405). If marked, provide justification:**

96. Assent of Children *(check one only)***:**

☐ **The assent of each child who is capable of providing assent based on age, maturity, and psychological state will be sought.**

☐ **The assent of each child will not be sought because the capability of all of the children in this study population is so limited that they cannot reasonably be consulted. Explain why the capacity is so limited, e.g., age, maturity and/or psychological state:**

☐ **The assent of each child will not be sought because the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research. Explain what the direct benefit may be and why it is only available in the context of the research:**

Section 14 – Other

97. Please describe any other study procedures not referenced in the previous sections:

☒ **Not applicable**