

AWARD NUMBER: W81XWH-15-1-0294

TITLE: 4-drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty Analgesia in Veterans

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14. ABSTRACT During the research period, all team efforts entailed the management of regulatory requirements. These included: (i) Food and Drug Administration Investigational New Drug (FDA-IND) Application, review, revision/resubmission, and approval, (ii) University of Pittsburgh Institutional Review Board (IRB), (iii) VA Pittsburgh IRB, (iv) University of Pittsburgh Research Conduct and Compliance Office, (v) VA Pittsburgh Research and Development Quality Assurance, (vi) University of Pittsburgh Data Safety Monitoring Board, and ultimately (vii) DOD Human Research Protection Office (HRPO) review and approval. The FDA-IND process included the determination of safety of the 4-drug nerve block mixture; these proceedings led to an accepted manuscript in a peer-reviewed journal. Throughout this time, all study-related infrastructural issues were addressed, managed, and finalized, including case report forms, computer-based data entry and management via the REDCap system, and formulation of the Manual of Operating Procedures.					
15. SUBJECT TERMS Bupivacaine, clonidine, buprenorphine, dexamethasone, nerve block, pain, hip, knee					
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Table of Contents

	<u>Page</u>
1. Introduction	4
2. Keywords.....	4
3. Accomplishments.....	5
4. Impact.....	7
5. Changes/Problems.....	8
6. Products.....	9
7. Participants & Other Collaborating Organizations.....	10
8. Special Reporting Requirements.....	11
9. Appendices.....	
Quad Chart (1 page)	
Publication: <i>Pain Medicine</i> (9 pages)	
Manual of Operating Procedures (225 pages)	

1. Introduction

For joint replacement, single-injection nerve blocks with local anesthetics are simple to perform, but only provide 12-16 hours of pain relief that includes muscle weakness. This study will evaluate an innovative 36-hour single-injection nerve block that combines a low-concentration local anesthetic with other pain relievers injected near the nerve. In veterans undergoing total hip or knee replacement, we will compare single-injection nerve blocks with the plain local anesthetic bupivacaine against a 4-drug combination (including bupivacaine) in veterans undergoing hip or knee replacement surgery. The other 3 drugs are clonidine-buprenorphine-dexamethasone (CBD). Based on these two treatments, the goals are to determine differing effects on (1) pain; (2) physical function; (3) discharge plans after hospital care; (4) satisfaction with treatment and emotional response; and (5) symptoms and adverse events. These outcome domains will be measured using both validated and innovative methods. Preoperative baseline survey data will be collected, and patient-follow-up will take place during days 1-4, and at 2 and 6 weeks after surgery. This research is projected to take approximately four years. We project that the 36-hour single-injection 4-drug nerve block will have immediate military relevance, by reducing or eliminating the complexity involved with inserting nerve block catheters in injured soldiers in or near the battlefield before lengthy transport to definitive medical care.

2. Keywords

Bupivacaine, clonidine, buprenorphine, dexamethasone, nerve block, pain, hip, knee

3. Accomplishments

Section 3.1: MAJOR GOALS

Task 1. Administrative, infrastructural, and regulatory affairs: FDA IND submission, review, response, and approval of the full IND.

Task 2. Related to funding-dependent infrastructural and enrollment activity

Task #2a: Administrative, infrastructural, and regulatory affairs: VA Pittsburgh Healthcare System (VAPHS) Institutional Review Board (IRB) submission / revision / approval; creation of Data Safety Monitoring Board DSMB through Pitt; VAPHS office setup; credentialing Pitt-hired research team members at VAPHS; VAPHS physical therapy team finalizing the research template with Pitt-hired physical therapists.

Task #2b: Hire, train, and credential physical therapists/recruiters (hired through University of Pittsburgh)

Task #2c: Study-specific programming and preparation for, communications, data collection, and data management: finalize Case Report Forms, purchase and programming of laptop PCs.

Task #2d: Screening, enrollment, baseline data collection, randomization, surgery, hospitalization

Task #2e: Study participant follow-up for six weeks after surgery

Task #2f: Periodic regulatory surveillance (IRBs / HRPO, Pitt DSMB, DoD Quarterly/Annual Reports, FDA-IND)

Task 3. Related to scholarly tasks of transforming data into information

Task #3a: Ongoing data entry quality verification

Task #3b: Periodic data analyses for professional meeting presentations and DoD annual reports

Task #3c: Data reduction, analysis, and interpretation; manuscript preparations, presentations, revisions, and publications

Task #3d: Active dissemination of research findings via relevant professional societies

Section 3.2: ACCOMPLISHMENTS UNDER THESE GOALS

Task 1: This task entailed the management of regulatory requirements that evolved after award announcement, specifically the FDA Investigational New Drug (IND) application process (folio #127171, initiated June 2015, ultimately approved 7 December 2015, with two separate iterative replies required). The primary concern was gaining either exemption or approval for our FDA IND application. Our initial application required an IND since three drugs in the 4-drug nerve block (clonidine-buprenorphine-dexamethasone) are not FDA-approved for perineural use, although each of the three drugs have been used (off-label) via the perineural route dating back as early as the 1980s. Our initial application included drug mixture safety data generated from our NIH (*in vitro*) and DoD (*in vivo*) funded studies, and associated publications. Our first response to the FDA-IND reply required a patient-safety report (n=1830 patients with the 4-drug nerve blocks as part of an institutional clinical pathway) from within our institution describing patient safety. Our final FDA-IND response required an evaluation of endotoxin risk and microbial risk when mixing these drugs in the clinical environment where our study will be taking place: all microbial growth was negative, and all endotoxin evaluations were negative. This FDA approval (not exemption) was sent to us on 7 December 2015.

Other achievements related to this FDA-IND task was the submission of two peer-reviewed manuscripts that were formulated based on the described requirements. One was published (ePub ahead of print), and the other was accepted for publication. Both involved the journal *Pain Medicine*.

- Williams BA, Ibinson JW, Gould AJ, Mangione MP. The incidence of peripheral nerve injury after multimodal perineural anesthesia/analgesia does not appear to differ from that following single-drug nerve blocks (2011-2014). *Pain Medicine* 2016; doi: 10.1093/pm/pnv107
- Williams BA, Podnar SM, Bonant SA, Schanck AM. TECHNICAL COMMUNICATION: Admixture of bupivacaine-clonidine-buprenorphine-dexamethasone at the bedside in a tertiary care hospital block room is not associated with any apparent burdens of endotoxin or microbial growth. *Pain Medicine* 2016, accepted for publication, Manuscript ID PME-OTH-Jun-16-449.R1

Task 2. These tasks were related to funding-dependent infrastructural and enrollment activity. Tasks 2a, 2b, and 2c are complete. Tasks 2d, 2e, and 2f are all related to active recruitment and protocol implementation, and associated periodic regulatory surveillance (and ongoing procedures to ensure all activities being accurately tracked and easily accessible for future audit purposes).

The primary accomplishment over the 17-month period (dating to the funding announcement but initiated before actual funding) was the cross-management of separate regulatory requirements within the relevant local institutions (University of Pittsburgh [hereafter “Pitt”] and VA Pittsburgh). These included but were not restricted to: (i) Pitt IRB (folio# PRO 15070157, initiated August 2015), (ii) VA Pittsburgh IRB (folio# PRO 1357, initiated July 2015), and (iii) Pitt Data Safety Monitoring Board (DSMB) (folio # IDSMB #00068, initiated September 2015). Of special interest is that (i) these entities were unable to provide final approval until the FDA-IND was approved, (ii) Pitt Office of Research forbade the release of funds until there was an approved IRB application, (iii) and both Pitt and VA IRBs required additional internal regulatory processes beyond those required by the DOD and the FDA (for the IND). After this complexity, we were ultimately able to make our initial submission for the DOD HRPO USAMRMC review, submitted 21 March 2016. Amendments were required that needed to undergo additional approvals by Pitt and VA Pittsburgh IRBs.

In May 2016, an unavoidable methodological barrier (described in our 3rd Quarter report) was identified by the Pitt-based lead co-investigator Sara Piva, PhD in collaboration with the VA Pittsburgh-based physical therapists. This barrier was addressed over ensuing weeks, leading to another required layer of cross-institutional coordinated approvals. Once these approvals were achieved, the final revised document for the DOD HRPO USAMRMC review was submitted. Initial DOD HRPO USAMRMC email approval was sent to us on 21 September 2016, and directives to start recruiting were issued in ensuing days.

There is one final regulatory process worth mentioning that occurred between the final IRB amendment submissions and IRB approvals by Pitt and VA Pittsburgh. This involved the Pitt Education and Compliance Office (Pitt ECO), an entity within the Pitt Research Conduct and Compliance Office (RCCO). The Pitt ECO was enlisted at the directive of the University of Pittsburgh IRB to ensure study compliance related to the protocol involving an FDA IND. The Pitt ECO directed our research team to have a “Site Initiation Visit” (SIV) before the start of participant recruitment; the SIV occurred on 11 August 2016. We now confidently declare that screening and participant recruitment will be underway, and that participants will be enrolled, *en route* to near-future joint replacement surgery and study protocol execution during hospitalization. From there with accumulation of study participant data, we will be able to embark upon **Task 3**.

Section 3.3: OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT

Nothing to report

Section 3.4: HOW THE RESULTS WERE DISSEMINATED

We consider ourselves fortunate that the peer-reviewed journal *Pain Medicine* was interested in the subject matter that we were required to evaluate for the FDA-IND application. The two manuscripts that were transformed from FDA-IND responses to peer-reviewed manuscripts are listed above. Otherwise, nothing to report.

Section 3.5: PLANS DURING THE NEXT REPORTING PERIOD

Based on our approved status, we will be able to fully engage in Tasks 2d, 2e, 2f, and 3 throughout the next reporting period. All teams, including research coordinators, physicians, physical therapists, allied health personnel, and clinical / research support staff teams are now all engaged in their study-specific duties. The Manual of Operating Procedures for the study has been distributed to all team members.

4. Impact

“Nothing to Report” applies to the following sections:

Section 4.1: IMPACT ON THE DEVELOPMENT OF THE PRINCIPAL DISCIPLINE

Section 4.2: IMPACT ON OTHER DISCIPLINES

Section 4.3: IMPACT ON TECHNOLOGY TRANSFER

Section 4.4: IMPACT ON SOCIETY BEYOND SCIENCE AND TECHNOLOGY

5. Changes / Problems

Section 5.1: CHANGES IN APPROACH AND REASONS FOR CHANGE

and

Section 5.2: ACTUAL OR ANTICIPATED PROBLEMS OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

For readers of this report that are considering a similar pursuit, there is one major regulatory event that led to a significant change in approach to gaining final approval to conduct the study. In our initial application for this grant, there were no stipulations that FDA approval of an Investigational New Drug (IND) application would be required, with respect to the use of drugs that are already on the market in the United States. As background, our 4-drug nerve block is comprised of bupivacaine, clonidine, buprenorphine, and dexamethasone. At our clinical institution (VA Pittsburgh), we gained hospital Medical Executive Board approval to use this 4-drug nerve block, “off label”, before our nerve block program began in mid-2011. It should be noted that the VA Pittsburgh IRB (unlike the instructions on the DOD grant application) required FDA IND approval before approving the described study. We are unaware if the Pitt IRB would have required FDA IND approval, other than they were already aware that the VA IRB required FDA IND approval. When we submitted the original FDA IND application, we included an outcomes manuscript of our center’s “off label” use of the 4-drug combination in nerve blocks, as well as rat safety data *in vitro* and *in vivo* (as peer-reviewed publications generated from research sponsored by the NIH and the DOD). The outcomes publication addressing the “off-label” use of the 4-drug combination entailed over 1300 nerve blocks over a 3-year period. Interestingly, the 1300 nerve blocks publication, along with the initial submission of the other animal data manuscripts, was not sufficient to gain FDA IND approval; we were required to query hospital charts of over 1800 patients to further demonstrate safety of the 4-drug combination. This process took an extended period of time and professional effort. Whether DOD research officials could potentially engage in cooperative discussions with the FDA for regulatory modifications addressing already-marketed drugs, and involving investigator-sponsors as opposed to drug company sponsors, may be of possible long-term value for this avenue of research.

Section 5.3: CHANGES THAT HAD A SIGNIFICANT IMPACT ON EXPENDITURES

The situation described above led to PI salary expenditures in isolation that could not be accompanied by salary expenditures of other team members charged with facilitating the start of the research protocol (since protocol approval was pending the FDA-IND approval). We are unable to determine whether this change will have a sufficiently significant impact on expenditures as to adversely affect future study salaries/processes “downstream.”

Section 5.4: SIGNIFICANT CHANGES IN USE OR CARE OF HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

Animals, biohazards, and/or select agents are not applicable.
There were no significant changes in the care of human subjects.

6. Products

Section 6.1: Publications, conference papers, and presentations

- Williams BA, Ibinson JW, Gould AJ, Mangione MP. The incidence of peripheral nerve injury after multimodal perineural anesthesia/analgesia does not appear to differ from that following single-drug nerve blocks (2011-2014). *Pain Medicine* 2016; doi: 10.1093/pm/pnv107
- Williams BA, Podnar SM, Bonant SA, Schanck AM. TECHNICAL COMMUNICATION: Admixture of bupivacaine-clonidine-buprenorphine-dexamethasone at the bedside in a tertiary care hospital block room is not associated with any apparent burdens of endotoxin or microbial growth. *Pain Medicine* 2016, accepted for publication, Manuscript ID PME-OTH-Jun-16-449.R1

Both of these acknowledged DoD support,
although these costs were incurred before funding was released.

Books / other: Nothing to report

“Nothing to Report” applies to the following sections:

Section 6.2: WEBSITES

Section 6.3: TECHNOLOGIES / TECHNIQUES

Section 6.4: INVENTIONS / PATENTS / LICENSES

Section 6.5: OTHER

7. Participants & Other Collaborating Organizations

Section 7.1: INDIVIDUALS THAT HAVE WORKED ON THE PROJECT

Name: *Brian A. Williams, MD, MBA*
 Project Role: *PI / PD*
 Researcher Identifier (e.g. ORCID ID): *TBD*
 Nearest person month worked: *5*
 Contribution to Project: *Dr. Williams has managed the activities as described above.*

Name: *Sara R. Piva, PT, PhD*
 Project Role: *Lead co-investigator for physical therapy / rehabilitation*
 Researcher Identifier (e.g. ORCID ID): *TBD*
 Nearest person month worked: *3*
 Contribution to Project: *Dr. Piva has coordinated all activities related to physical therapy care and assessment, including hiring and training of physical therapists, developing documents for data collection, manual of operations, and overseeing regulatory paperwork related to physical therapy care and assessment.*

Name: *Samantha Bonant, MS, CCRP*
 Project Role: *Regulatory Specialist Coordinator*
 Researcher Identifier (e.g. ORCID ID): *TBD*
 Nearest person month worked: *6 (originally forecasted as 0.9)*
 Contribution to Project: *Ms. Bonant handles all regulatory submissions, including IRB, FDA, IDSMB and DoD submissions.*
 Funding Support: *Veterans Research Foundation of Pittsburgh, plus DOD sponsorship.*

Name: *Karen Gilbert*
 Project Role: *Study Coordinator*
 Researcher Identifier (e.g. ORCID ID): *TBD*
 Nearest person month worked: *12*
 Contribution to Project: *Ms. Gilbert is the lead coordinator, and was responsible for constructing the Manual of Operating Procedures, among many other coordination and educational activities*
 Funding Support: *Veterans Research Foundation of Pittsburgh, plus DOD sponsorship*

Section 7.2: CHANGES IN THE ACTIVE OTHER SUPPORT OF THE PD/PI(S) OR SENIOR/KEYPERSONNEL

Nothing to report

SECTION 7.3: OTHER ORGANIZATIONS INVOLVED AS PARTNERS

Nothing to report

8. Special Reporting Requirements

See attached Quad Chart

9. Appendices

- Quad Chart
- In-press manuscript
- (the accepted-for-publication manuscript is not ready for public distribution, per the publisher)
- Manual of Operating Procedures (which includes all case report forms)

4-Drug Nerve Block vs Plain Local Anesthetic for Knee & Hip

Log Number: 13232002 – Prospective Randomized Clinical Trial at the VA Pittsburgh

Award Number: W81XWH-15-1-0294



PI: Brian A. Williams, MD, MBA

Org: The University of Pittsburgh

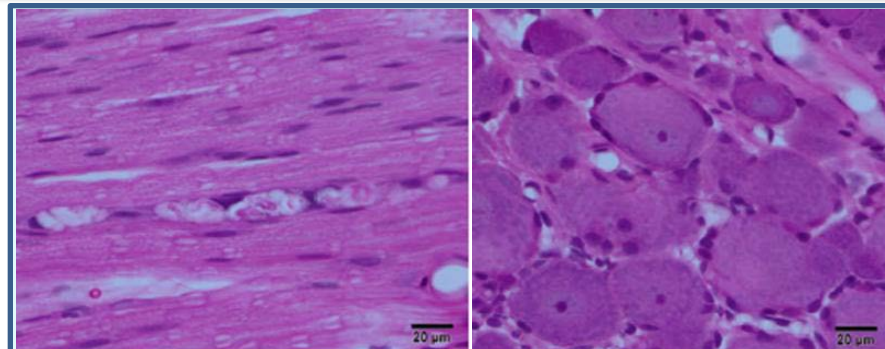
Award Amount: \$1,950,591.00

Study/Product Aim(s)

- Demonstrate analgesic superiority of 4-drug nerve block after elective joint arthroplasty when compared against single-injection nerve blocks with plain bupivacaine
- Determine whether this analgesic superiority postoperatively translates to equal or superior physical therapy outcomes
- Also track all study participants with validated outcome surveys, to quantify veteran-centered clinical outcome measures
- Military relevance: Is the described 4-drug single-injection nerve block sufficiently robust to reconsider current nerve block continuous infusions that are complex to insert and maintain in the battlefield theater (Level 3, possibly earlier)?

Approach

Prospective randomized triple-blinded clinical trial of n=200 veterans undergoing knee (n=100) or hip (n=100) replacement.



In previous DoD-funded in vivo rat studies, the 4-drug nerve block was equally safe to the nerve as was plain bupivacaine

After due diligence in rat studies *in vitro* and *in vivo*, we have gained FDA approval of our IND application, and IRB approval, to evaluate the 4-drug single-injection nerve block (bupivacaine-clonidine-buprenorphine-dexamethasone) in Veterans.

Timeline and Cost

Activities	CY	16	17	18	19
Regulatory (FDA / IRB) / infrastructure					
Screening, enrollment, study-specific hospitalization					
One-month study participant follow-up					
Ongoing regulatory issues, and scholarly output					
Estimated Budget (\$K)		\$587	\$545	\$557	\$262

Goals/Milestones

CY16 Goal – Regulatory approvals and study enrollment

☒ FDA-IND approval. IRB approvals. Study staff/ infrastructure.

☒ USAMRMC HRPO revisions approved.

☒ Subject screening/enrollment – begin 9/26/2016

CY17 Goals – Study enrollment and regulatory updates

☒ Participant screening (enrollment just underway 10/25/16)

☐ Data integrity, interim safety analysis, regulatory updates

CY18 Goal – Study enrollment and regulatory updates

☐ Participant screening and enrollment

☐ Data integrity, interim safety/efficacy analysis, regulatory updates

CY19 Goal – Finish study enrollment, scholarly output

☐ Submit manuscripts for peer-reviewed publication

Comments/Challenges/Issues/Concerns

- Coordinating documents and approvals of VA, Pitt, and USAMRMC

Budget Expenditure to Date

Projected Expenditure: \$586,991 (subject enrollment was projected)

Actual Expenditure: \$365,734 (all pre-enrollment)

Updated: Pittsburgh, PA; 25 October 2016

Commentary

The Incidence of Peripheral Nerve Injury After Multimodal Perineural Anesthesia/Analgesia Does Not Appear to Differ from That Following Single-Drug Nerve Blocks (2011–2014)

Introduction

Recently, we reported on the *in vitro* [1] and *in vivo* [2] animal safety (rat) of four-drug nerve block (multimodal perineural anesthesia–analgesia, or MMPNA) combinations involving bupivacaine (BPV [2]), ropivacaine (RPV [1]), or midazolam (MDZ [1,2]) with the following three preservative-free injectable drugs: clonidine, buprenorphine, and dexamethasone [1,2] (hereafter abbreviated as CBD). In addition, we provided clinical benchmark data for patients having received nerve blocks with combined BPV-CBD [3] and MDZ-CBD [4]. The chronological time frame for these previous clinical benchmark reports [3,4] was July 2011 through March 2014. The current report covers intermediate and long-term peripheral nerve injury (PNI) outcomes for $n = 1830$ patient-block encounters dating from July 2011 through December 2014.

We define a “patient-block encounter” as a uniquely identified patient encounter receiving one or more nerve blocks on a specific day for pre- and intra-operative anesthesia/analgesia, immediate postoperative analgesia, or rescue postoperative analgesia on a day after surgery, typically during the same hospital stay. The blocks used for these 1830 patient-block encounters were composed primarily of BPV-CBD ($n = 1726$; 94.3%), or MDZ-CBD ($n = 104$; 5.7%). Patients who were having surgery related to a current or previous surgical site infection typically did not have blocks that included perineural dexamethasone ($n = 109/1830$, or 6%).

The objective of this report is to present complication-related quality improvement (QI) data from our institution in the epidemiologic context of such data published elsewhere regarding the risk of PNI complications related to surgery itself (without specific nerve block considerations) or specifically related to nerve blocks typically using local anesthetics only (in the absence of multiple or any perineural adjuvants).

In our institution (Veterans Affairs Pittsburgh Healthcare System, VAPHS), the lead author was charged with creating a regional anesthesia (RA) and analgesia program

for patients eligible for peripheral nerve blocks. The VAPHS Medical Executive Board approved the lead author's recommendation to routinely use the described four-drug nerve blocks off-label. These single-injection nerve blocks are typically placed before surgery to provide postoperative analgesia and intraoperative anesthesia when feasible. Pursuant from institutional approval was the need to collect QI data prospectively (within 2 weeks after the block encounter) to evaluate dose-specific comparative effectiveness (block duration and rebound pain, which we previously reported [5,6]). Additional QI data were later collected retrospectively to determine perineural complications and to establish MMPNA safety. In accordance with Veterans Health Administration Handbook 1058.05, this manuscript was processed for authentication of nonresearch status of the described activities prior to submission to this journal. The VAPHS institutional review board declared these clinical operations “not research” at the time of program initiation (mid-2011) and annually since then during required reviews.

Methods

Definition of perineural complication. This medical record review identified patients who had EMG examinations after the date of the described patient-block encounter. Included was a review of the EMG consultation order, and the specific progress notes time-associated with the EMG order. The review also entailed the screening of postoperative notes by the surgical team following up on the patient for any notes indicating potential PNI symptoms that were traceable to the site of the needle injection for the performed blocks, but for which EMG was not ordered. This medical record review did not track complications (e.g., intraoperative hypotension, postoperative nausea/vomiting) other than neurologic symptoms in the distribution of the surgery and/or nerve block(s).

Patient selection for data analysis of QI-reportable occurrences, and data collation. From July 1, 2011 through December 31, 2014, there were $n = 1830$ patient-block encounters

involving MMPNA in an all-inclusive QI database. For QI purposes, electronic medical records with patient identifiers for cases 1 through 800 were screened by author AJG, including postoperative notes by the surgical team and/or any other relevant progress notes (e.g., neurology, physical medicine and rehabilitation) that may have indicated possible PNI outcomes. In addition, all electronic medical records were screened for any EMG testing procedures that were done before or after the index MMPNA patient-block procedure-encounters. After screening, author AJG provided a summary list to the lead author (BAW) for a detailed QI review of these cases to determine the relationship of the EMG reports to the needle location of the block performed and the symptoms for which the postoperative EMG was ordered to specifically evaluate. The presence of preoperative or postoperative spine problems was evaluated by the lead author to determine the relationship of spine pathology level to previous or future QI issues (e.g., cervical spine abnormality that was diagnosed before versus brachial plexus-based patient complaint after having undergone a brachial plexus block). For patients in whom EMG was not ordered, the lead author reviewed the electronic medical record details involving preoperative symptoms, timing of onset of postoperative symptoms, operative notes, coinciding spine pathology, and timing of symptom resolution, if applicable. For cases 801 through 1830, the lead author was responsible for both screening and conducting a detailed review of all records. In other words, all 1830 patient-block encounter medical records were reviewed not only for the presence of any EMG testing, but also for the presence of potential PNI symptoms without evidence of EMG testing.

The following block types were recorded during QI data-sheet collation: (i) brachial plexus below the clavicle (typically axillary), (ii) brachial plexus above the clavicle (typically interscalene or supraclavicular), (iii) L2–L4 only (i.e., psoas compartment, femoral, or saphenous), (iv) L2–L4 and L4–S3 in which the L2–L4 block was specifically at the level of the psoas compartment, (v) L2–L4 and L4–S3 in which the L2–L4 was specifically of the femoral nerve in the groin, and (vi) popliteal sciatic with or without a separate saphenous nerve block (i.e., specifically for foot-ankle surgery). The timing of EMG testing was recorded as follows: (i) no pre- or postoperative EMG testing of the relevant nerve distribution, (ii) only preoperative EMG testing without postoperative EMG testing, (iii) postoperative EMG testing without any preoperative EMG testing, and (iv) both preoperative and postoperative EMG testing. For any postoperative EMG testing, we specified in our collated dataset if the electronic medical record indicated that the ordering provider (e.g., surgical team) mentioned in the medical record a specific concern about the nerve block as the reason for the EMG referral (i.e., no-yes dichotomous variable). Dichotomous variables were assigned accordingly if an identified EMG lesion correlated with the needle location for the block used. Patients were not contacted as part of this QI review. However, if the

surgical team deemed it appropriate, they notified the anesthesia service on a discretionary basis of any possible complications of which they felt the anesthesia service needed to be aware, and such notification may have involved the anesthesia care team member contacting the patient as part of the care process and follow-up.

Coinciding 30-day mortality data from the Veterans Affairs Surgical Quality Improvement Project (VASQIP[7]), 2006–2014. The VA National Surgery Office (NSO) publishes a quarterly report to provide the Veterans Integrated Service Network (VISN) Surgical Work Group and Facility Surgical Work Groups, as defined in Veterans Health Administration (VHA) Handbook 1102.01, with a standardized set of surgically relevant information upon which to evaluate local and VISN surgical delivery systems, best practices, and the overall quality of surgery services. The NSO Quarterly Report is designed to facilitate a community of surgical practice and the delivery of high-quality and timely surgical services to our nation's veterans. For this manuscript, we will present only 30-day VASQIP morbidity and mortality data originating from the Orthopedics category at VAPHS. Of note, for VASQIP NSO quarterly reports, orthopedic mortality may have included orthopedic spine or other cases for which regional anesthesia was not an available care option. In addition, VASQIP NSO quarterly reports involve the comparison of a single VA hospital (e.g., VAPHS, and an "observed 30-day mortality") against aggregate VA nationwide data ("expected 30-day mortality") in creating "observed-to-expected" 30-day morbidity and mortality ratios. One limitation of VASQIP mortality data is that all 30-day mortalities are captured in the numerator, but not all survivals are captured in the denominator (as VASQIP represents a minimum sampling per institution that is to include all morbidities/mortalities in the numerator). Therefore, we will present quarterly trend data for VAPHS orthopedics before and after the start of our MMPNA nerve-block service. We will perform associated (i.e., association, not causation) statistical analyses of before and after aggregate data (30-day O-E mortality ratios) with the understanding that the mortality ratios for both "observed" and "expected" do not include the full denominator of surgical survivors.

We also tracked elective joint replacement mortalities throughout the 2006–2014 period (with complete denominators), and compared before and after the Acute Pain Medicine/Regional Anesthesia specialty service was inaugurated in July 2011.

Statistical Analyses

As a retrospective review of a QI database not originally intended for scientific/extramural reporting, there were no detailed analysis plans *a priori*. Descriptive statistics (proportions, 95% confidence intervals) are provided, and associated conclusions are presented as simply a comparison of our 95% confidence intervals against complication rates reported in the literature.

For the O-E 30-day morbidity/mortality ratios, raw ratios between zero and one were translated as “lower than national VA trend,” while raw ratios greater than one were translated as “higher than national VA trend.” However, as these raw ratios varied from greater than one to less than one, we were required to transform the raw ratio data to establish a “true zero.” To do so, each raw ratio data point was squared (i.e., raised to the second power) for proportional comparisons of the O-E ratio.¹ Mortality data were then compared before versus after the Acute Pain Medicine/Regional Anesthesia Service was established (2006 through June 2011, then July 2011 through December 2014) using the student’s t-test.

For the “before–after” absolute mortality calculations after elective joint replacement surgery (knee and hip, with known case denominators), associated differences in this outcome were evaluated using the Fisher’s Exact Test. These O-E data and before–after joint replacement mortality data were analyzed with IBM SPSS v21 statistical software (IBM SPSS®, Chicago, IL).

Results

Total encounters, and categorizing blocks for surgery versus blocks for analgesia. From July 1, 2011 until December 31, 2014, there were a total of 1830 patient-block encounters involving the Acute Pain Medicine/Regional Anesthesia Service utilizing MMPNA. Of note, 51% (n=937) of these blocks were used for “surgical anesthesia” (involving a higher concentration of local anesthetic to provide operating conditions not requiring other general or regional anesthesia). The remainder were typically designed for “postoperative analgesia,” meaning that the block was also combined with a spinal anesthetic (n=685; 77%) or a general anesthetic (i.e., with a secured airway, n=210; 23%) to achieve necessary surgical conditions. Most (n=1748; 96%) blocks were placed before surgery, and most patients (n=1339; 73%) were nondiabetic at the time of the block.

Types and timing of blocks performed, and postoperative frequency of EMG testing. The types of blocks performed are categorized in Table 1.

Of the EMG reports available on the computerized medical records for the patients associated with these n=1830 patient-block encounters, (i) n=242 EMGs were performed only before the surgery/block, (ii) n=58 EMGs (n=34 lower extremity and n=24 upper extremity) were performed only after the day-of-surgery/block, and (iii) n=15 had EMGs both before and after the surgery/block (n=14 of these were upper extremity surgery-blocks, and one was foot-ankle). The EMG studies performed only before the surgery/block (n=242) were excluded from subsequent analysis, and n=73 EMGs were included for analysis. Four of these 73 EMGs were repeat postoperative EMGs, so there were 69 total patients with any postoperative EMG.

There were n=38 upper extremity patient EMGs, and n=35 lower extremity patient EMGs (73 EMGs total across 1830 patient-block encounters, or 4%). Of the 73 total patient-block encounter EMGs, n=54 were nondiabetic and n=19 were diabetic.

Electronic medical records were reviewed for the 69 patients who underwent the total of 73 postoperative EMG evaluations. Before the EMGs were performed, 13 of the patient-specific EMG order/consultations indicated concerns specifically relevant to the nerve block performed. The other 56 patients’ EMGs were ordered for reasons in which no concern regarding the nerve block was specified; 55 of these 56 patients’ EMG reports did not indicate any findings suggestive of a lesion traceable to the nerve block injection, but one of these reports was unable to rule out a possible specific PNI case (not necessarily traceable to the block site) distinguished from long-standing preoperative pathology attributable to the lumbar spine (and previous spine surgery). Therefore, of 13 EMGs specifically ordered to address nerve block concerns, 2 were “definite” PNI cases (2/1830, or 0.11%), and 4 were “possible” PNI cases. Adding the 1 “possible” PNI case from the 56 EMGs ordered (unrelated to block concerns) leads to 2 “definite” and 5 “possible” (from the 13 EMGs concerned with the nerve block) and yields an incidence of 7/1830 (0.38%) “definite or possible” PNI.

EMG Case Details

Popliteal (with or without saphenous, n=328). Of the seven numerator patients with definite or possible lesions on EMG, one had a popliteal-saphenous block for surgical anesthesia and a definite PNI lesion (“definite POP,” 1/328, 0.3%, 95% CI: 0.05%, 1.7%) and one had a possible PNI popliteal-saphenous analgesic block combined with a spinal (“possible POP-SPI” case, with cumulative popliteal risk being 2/328, 0.6%, 95% CI: 0.17%, 2.20%). The definite POP case (who was not diabetic and had no previous symptomatic complaints) on the postoperative EMG was found to have profound bilateral peripheral lower extremity neuropathy, and a presumably new lesion traceable to the block needle in the popliteal fossa. It is conceivable that this case may have instead involved postoperative bilateral inflammatory neuropathy after one-sided surgery with regional anesthesia, as has been reported recently [8]. Meanwhile, the possible POP-SPI case had diffuse bilateral EMG findings, and a common peroneal EMG focus “of questionable significance.” The lumbar spine MRI of the possible POP-SPI case also showed some anatomic lesions unrelated to the block. The consulting neurologist ultimately ascribed a diagnosis of “intermittent sciatica” for the possible POP-SPI case.

Interscalene (n=278). One of the seven “definite or possible” patients had an interscalene block for surgical anesthesia (“possible ISB case,” 1/278, 0.4%, 95% CI: 0.06%, 2%). The ISB case manifested as a winged scapula postoperatively that was undocumented

Table 1 Totals per block procedure type (n = 1830 patient-block encounters overall), and definite/possible PNI cases based on EMG testing

Category	N
Axillary	315
• No definite or possible EMG cases	
Interscalene/supraclavicular	278
• One possible PNI case (see ISB)	
Femoral or psoas compartment	113
without L4–S3 block	
• No definite or possible PNI cases	
Psoas compartment lumbar plexus	494
plus L4–S3 block (i.e., 988 total blocks)	
For hip	300 (i.e., 600 total blocks)
• One definite L2–L4 PNI case (see HIP-LUM)	
• One possible L4–S3 PNI case (see HIP-PS)	
Caudal to hip	194 (i.e., 388 total blocks)
• Two possible L4–S3 PNI cases (see LUM-SCI knee and LUM-SCI ankle)	
Femoral and sciatic	298 (i.e., 596 total blocks)
• No definite or possible PNI cases	
Popliteal	328
with or without saphenous/femoral	
• One definite PNI case (see POP)	
• One possible PNI case (see POP-SPI)	
Other	4
• No definite or possible PNI cases	

PNI: peripheral nerve injury; EMG: electromyography.

See text for the individual case descriptions.

There were two definite cases of PNI (2/1830, 0.11%) and five possible cases of PNI (5/1830, 0.27%).

preoperatively. The occupational mechanism of injury leading to the need for the surgical procedure was an abrupt “heavy tugging” of a free-falling 300-lb (136-kg) weight on a pulley, resulting in a distal biceps rupture and a possibly undetected simultaneous isolated long thoracic nerve injury. We attribute the EMG finding to the mechanism of injury and not to the block, but still conservatively categorize the case as “possible.”

Lumbar plexus psoas compartment block with either parasacral or gluteal sciatic block (n = 494). Four of the remaining seven “definite or possible” patients had lumbar plexus blocks with either parasacral or gluteal sciatic L4–S3 blocks. Two of these four patients had spinal anesthesia with preoperative psoas compartment and parasacral blocks for hip surgery. One lesion was traceable to the lumbar plexus (“definite HIP-LUM”). The other lesion was traceable to the proximal sciatic nerve at the level of the long head of the biceps (“possible HIP-PS,” of questionable proximity of the parasacral injection site; the primary causative factor was indeterminate, but favoring surgical stretch over the injection site, perhaps in a “double crush” phenomenon). The third of four patients (“possible LUM-SCI knee”) had surgical lumbar plexus and gluteal sciatic anesthetic blocks for knee

replacement. The fourth of four patients (“possible LUM-SCI ankle”) had lumbar plexus and sciatic blocks for many ankle procedures. Therefore, the risk proportion calculation, given that this category includes two anatomically separate blocks, is: one “definite” case/494 patients, 0.2%, 95% CI: 0.07%, 0.6%; versus four “definite or possible”/494 patients, 0.8%, 95% CI: 0.28%, 2.4%). So in these 494 patients, 988 total blocks (excluding spinal) were performed; our 95% confidence intervals conservatively reflect “patients” (n = 494), not “blocks” (n = 988).

The definite HIP-LUM case had two normal EMGs at our hospital facility, reflecting a normal L2–L4 peripheral sensory exam, but two “second opinion” EMGs at outside hospitals performed paraspinous EMG/myography showing a profound lesion within the lumbar plexus itself that our hospital’s EMGs did not specifically test for.

The possible HIP-PS case first manifested symptoms 2 weeks postoperatively. The lesion was localized in the proximal sciatic nerve distribution, in that the long head of the biceps was affected during myography (failing to rule out surgical stretch), but the gluteal musculature was unaffected (less favoring a parasacral plexus needle

lesion). Therefore, the EMG was partially able to favor surgical stretch and partially rule out the focal needle injection site. This possible HIP-PS patient was reported to be a noncompliant diabetic, which may have complicated matters postoperatively (including the absence of symptoms until 2 weeks postoperatively), all of which factor against the PNI focus being the parasacral block injection site. The possible LUM-SCI knee PNI case (total knee replacement) had a known problematic lumbar spine, diabetes with peripheral polyneuropathy, and had recorded in the medical records a statement that he also encountered many of his postoperative symptoms preoperatively. There was no EMG myography testing for gluteal/hamstring evaluation for a complete evaluation of the sciatic nerve on the possible LUM-SCI knee patient, because this patient underwent EMG testing while therapeutically anticoagulated with warfarin.

The possible LUM-SCI ankle case was a diabetic who had previously undergone three major lumbar spine surgeries in our institution and seven foot/ankle procedures. In two separate postoperative EMG reports (in 2013 and 2014), the interpretation was unable to exclude a superimposed ipsilateral L5–S1 focal versus neuraxial radiculopathy, given a longstanding sensory-motor peripheral polyneuropathy with chronic axonal loss.

Conservative approach to expand the risk probability and its 95% confidence interval. In a separate chart review of patients not referred for EMG, there were seven cases of abnormal postoperative physical exam findings that were judged (by authors BAW and JWI) to be possibly block related, for which there was no EMG ordered to appropriately evaluate. Based on the proportions described above, we will assume that if these seven had had EMGs ordered, three may have proven to be positive. Therefore, in our conservative estimation, the risk of PNI from MMPNA injections that has been (or may be) traceable to the site of nerve block injection is 10/1830, or 0.55%. The 95% confidence interval of this incidence is 0.27% to 1.08%.

Coinciding 30-day orthopedic morbidity/mortality data from the Veterans Affairs Surgical Quality Improvement Project (VASQIP[7]), 2006–2014 (Figure 1). In January 2011, our institution implemented a new “preoperative optimization” program (“Interdisciplinary Medical Perioperative Assessment Consultation Treatment,” abbreviated as IMPACT) that can be summarized as reasonably equivalent to the advances described in the literature addressing perioperative surgical homes [9]. In July 2011, the regional anesthesia team was created, but was not fully operational on a daily basis until February 2012. Before the creation of the IMPACT program and regional anesthesia team, the overall O-E ratios for morbidity and mortality were 1.18 (1.04, 1.33) and 1.24 (0.93–1.59), respectively. After the regional anesthesia team was created and through December 2014, the O-E ratios were 0.72 (0.50, 0.97) and 0.22 (0.00, 0.74; $P = 0.001$ for

both morbidity and mortality, respectively, based on the t-test). These values represent (based on transformed ratio statistics to a common zero) reductions in observed-to-expected morbidity and mortality ratios of 22% and 58%, respectively. We were statistically unable to delineate morbidity/mortality reductions traceable specifically to the perioperative surgical home equivalent versus the effect of near-ubiquitous regional anesthesia and reduction in GETA use. Unfortunately, we were also unable to track proportions of complicated patients that were elective orthopedic procedures (e.g., TKA, THA, with full surgical-home equivalent workup 2011–2014) versus emergency procedures (e.g., hip/femur fracture repair with no elective workup and health status optimization). Therefore, we are unable to speculate about the trade-off of PNI complications with the advent of the new block team (we do not have PNI data from 2006–2012 during the GETA-only era) in exchange for reduced 30-day mortality (as we are unable to delineate reduced mortality as being from GETA avoidance versus better preoperative selection and optimization), but we include our “before-after” mortality data in an effort to allow other research teams to generate hypotheses and calculate sample sizes.

Coinciding 30-day orthopedic mortality data after THA and TKA from institutional data, 2006–2014 (Table 2). From 2006–2010, there were three TKA 30-day mortalities (2006, 2009, 2010) and three (two in 2008 and one in 2010) THA 30-day mortalities. There were no THA/TKA 30-day mortalities from 2011 through 2014 ($P = 0.014$, by Fisher’s Exact Test).

Discussion

The complexities of forecasting the risk of PNI, irrespective of neurolocation technique, have recently been published (2015) in the Second Practice Advisory of the American Society of Regional Anesthesia and Pain Medicine [10]. For common PNB techniques entailing the use of plain local anesthetics, the rates of PNI after interscalene brachial plexus block, axillary brachial plexus block, and femoral nerve block have been reported as 2.84% (95% CI: 1.33–5.98%), 1.48% (95% CI: 0.52–4.11%), and 0.34% (95% CI: 0.04–2.81%), respectively, based on detailed review of prospective randomized studies to date as of 2007 reported by Brull et al. ($n=10,309$) [11]. In a single-institution study (Fredrickson and Kilfoyle [12]) of 1010 consecutive peripheral nerve blocks with plain local anesthetics, new, all-cause, neurological symptoms were present in 56/690 blocks (8.2%; 95% CI: 6.8–10.2%) at day 10, 37/1010 (3.7%; 95% CI: 2.7–5.0%) at 1 month, and 6/1010 (0.6%; 95% CI: 0.27–1.3%) at 6 months [12]. Most symptoms in this [12] study were due to causes unrelated to the block: 4 of 1010 were ultimately unrelated to the block, but for the other 2/1010 (0.2%), attribution to the block could not be ruled out. In another

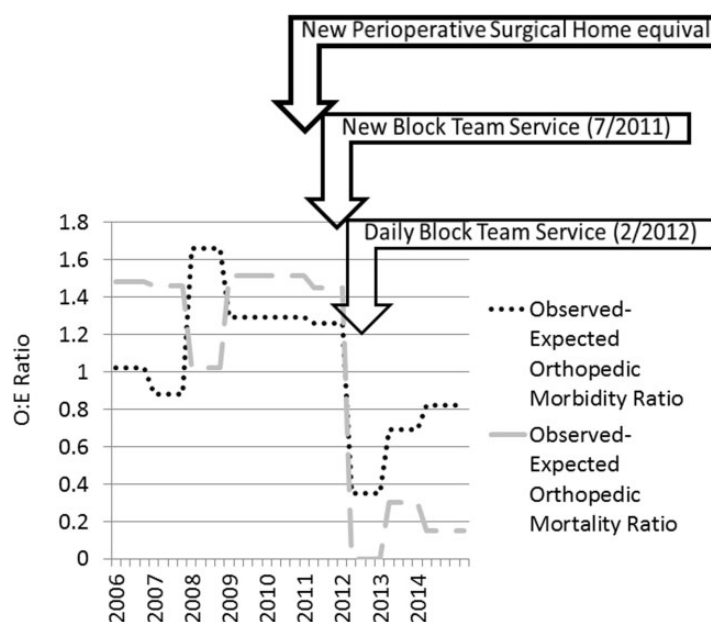


Figure 1 Reductions in institutional orthopedics morbidity and mortality observed-to-expected ratios. The X-axis represents the timeline of 2006–2014 orthopedics cases performed at the VA Pittsburgh Health System. The Y-axis O:E ratio represents the observed-to-expected ratio of morbidity (dotted black line) and mortality (dashed gray line) for tracked cases in quarterly VASQIP reports from the VA Central National Surgery Office (see text for details). The “observed” value represents actual complications observed during a quarterly audit (at VA Pittsburgh), which is compared with “expected” complications based on the same summed quarterly audit of all VA hospitals nationwide. The ratio value of 1 indicates that the VA Pittsburgh morbidity/mortality rates match those of national trends for the same time period. Less than 1 indicates the VA Pittsburgh having better outcomes than those of national trends (a ratio of 0.5 indicates half the complication rate of national). Greater than 1 indicates the VA Pittsburgh having less satisfactory outcomes than those in national trends (a ratio of 2.0 indicates twice the complication rate of national). The timeline arrows at the top of the graph reflect the inauguration of the perioperative surgical home in January 2011, the start of the block team in July 2011, and the fully-staffed daily block team in February 2012. Note that all complications recorded are irrespective of hospital inpatient status (i.e., not routed through the perioperative surgical home equivalent, such as hip fracture patients) versus outpatient status (outpatients routed through the surgical home equivalent, such as for knee or hip replacement). Quarterly data are annualized for ease of interpretation. Based on the t-test, the before versus after *P* value of the O:E ratios were *P* = 0.001 for both morbidity and mortality (see text for details). No further statistical delineation of the effects of the surgical home versus block team was possible.

study, the Australasian Collaboration (Barrington et al. [13]) cites a PNI incidence of 0.04% and a 95% confidence interval of 0.08 to 1.1 per 1000 (0.008–0.11%); this study counted each block in the denominator (7156 blocks among 6069 patients). Watts and Sharma [14] reported a 0.22% PNI incidence (*n* = 1065 consecutive blocks over a 12-month period), while Laur et al. [15] reported a 0.32% short-term PNI incidence (*n* = 4363, 14 cases over a 15-month period).

We took a deliberate and conservative approach by (i) categorizing positive EMGs with questionable involvement of the needle location as potentially attributable to the block (in isolation or as part of a “double-crush” phenomenon) and (ii) adding three cases to the numerator (i.e., patients who did not have EMGs). These conservative tabulations led to our 0.55% risk estimate with

a 95% confidence interval of 0.27% to 1.08%. We are confident based on this detailed review of 1830 patient-block encounters that there were not any missed complications, with the exception of patient relocation or death (<1%). However, of the seven EMG-specific cases in the numerator, the following five cases are questionable at best for block-related PNI: POP-SPI, ISB, HIP-PS, LUM-SCI knee, and LUM-SCI ankle. Subtracting these five cases from the numerator, along with subtracting the theoretical three additional numerator cases that did not have EMG, yields a risk incidence of 2/1830 (0.11%), with a 95% CI of 0.03%–0.4%.

A frequent complex case under the auspices of our teaching institution’s Acute Pain Medicine/Regional Anesthesia service is elective total hip arthroplasty (THA, *n* = 237 in our data set). In literature review, the risk of

Table 2 Institutional 30-day mortality after THA/TKA from 2006 through 2014

Year	All THA	All TKA	Overall	30-day mortalities
2006	39	45	84	1 (TKA)
2007	62	81	143	
2008	57	89	146	2 (THA)
2009	63	91	154	1 (TKA)
2010	81	113	194	2 (THA and TKA)
Total: 0.8% 30-day mortality 2006–2010 (all GA)			721	6
2011	63	84	147	
2012	87	135	222	
2013	90	110	200	
2014	76	106	182	
Total: No 30-day mortalities in 751 cases, $P = 0.014$ by Fisher's Exact Test				

PNI (from all causes, not just those related to nerve blocks) from hip replacement ranges from 0.2% to 8% [16]. We had one lumbar plexus PNI case traceable to the injection site (definite HIP-LUM patient above), and one L4–S3 PNI case that did not involve the gluteal musculature on EMG, but did involve the long head of the biceps (possible HIP-PS patient above with uncontrolled diabetes). There was one other patient with postoperative symptoms (but no EMG) that were deemed to be possibly block related. There were also 19 THA patients with negative EMGs ($n = 4$), and no EMGs but L2–S3 symptoms ($n = 15$) not traceable to the block (based on surgical notes and/or procedural descriptions). So the overall THA PNI risk in our teaching institution was 9% (22/237, approximating the 8% range reported by Zappe et al. [16]). We consider our findings to be in a generally accepted risk range for rare complications after THA with proximal peripheral nerve blocks ($n = 1–3$ out of 237, 0.4–1.3%, for dual blocks of the lumbar and parasacral plexi).

Lumbar plexus blocks (in combination with parasacral blocks for hip surgery or in combination with gluteal sciatic blocks for lower extremity surgery distal to the hip) have the least available data regarding risk epidemiology. To our knowledge, the largest series reported to date entails 394 blocks performed in France during a voluntary hotline data collection report in a 10-month period from 1998–1999 ($n = 158,000$ blocks; lumbar plexus block-related major complication rate of 0.8% [17]). Our series of lumbar plexus blocks for surgical anesthesia and/or postoperative analgesia to date has since well surpassed $n = 500$ (July 2011–December 2014, $n = 494$). In our case series of $n = 494$ patients (through December 2014) having undergone lumbar plexus block, we reiterate from above that 13 patients had EMGs ordered that were specifically addressing postoperative concerns of the perioperative nerve block. Of these 13 patients, 7 had lumbar plexus blocks, with 4 being for hip replacement and 3 for knee replacement. In total, only one of the seven EMGs had plexus injury traced to the lumbar plexus needle injection site.

This was for hip surgery using an analgesic block with BPV-CBD.

During the July 2011–December 2014 time period, in addition to the 13 EMGs above that were ordered citing concerns with the perioperative nerve blocks, there were 56 other patients with EMGs ordered without specific mention of nerve block concerns. Of these 56, 5 patients had lumbar plexus blocks and none of these EMGs showed evidence of damage in proximity to the lumbar plexus site of injection (with one of these cases, LUM-SCI ankle, having a possible “unable to rule out” status). Therefore, 1/494 (0.2%; 95% CI: 0.04%–1.14%) of our patients having lumbar plexus blocks had definite PNI evidence per EMG at the site of injection.

Our overall objective of presenting these benchmark QI outcome data is to narrow down the scope of future research hypotheses involving MMPNA. Based on our institution's limited sample size in the context of the world's literature, we do not detect trends of PNI specifically traceable to the use of MMPNA in our institution when compared with all blocks performed worldwide using plain local anesthetics. As a QI-driven clinical activity, there are restrictions in data gathering and synthesis that forbid identifying preoperative/postoperative opioid requirements (e.g., related to possible PNI symptom management) and other factors related to general health status (i.e., “trade-off” of one set of possible complications [from peripheral nerve block] for another [from GETA]). None of our observations should be interpreted as suggestive for future (and acknowledged off-label) clinical practice. Due diligence in preclinical research has been done with respect to known neuronal safety (*in vitro* [1], CBD adjuvants) and more recently with respect to drug compatibility and *in vivo* safety in laboratory animals [2]. Previously published [3,4] in this journal is our report of associated block durations and rebound pain scores observed after these MMPNA blocks, but (as a clinical pathway) these outcomes were not compared with a plain local anesthetic control group. We reiterate that in the absence of an industry

sponsor, such research (or hypothesis generation for such research) would either occur slowly or not at all. Perhaps future research across several coordinated centers may help better delineate risk incidence (while narrowing the 95% confidence interval by increasing the sample size), although funding for such research (i.e., involving drugs that are no longer patent-protected, and not involving delineation of perineural mechanism of action) may not necessarily come from conventional sources beyond interinstitutional cooperation.

Conclusions

In this single-institution QI data review involving 1830 patient-block encounters entailing over 2600 blocks with multimodal perineural analgesia for either surgical anesthesia or postoperative analgesia, our patient-specific incidence of definite PNI was 0.11% (2/1830). When including possible PNI cases with EMG testing (n=5) and possible PNI cases that did not have EMG testing (n=3), our conservative estimate for PNI risk is 0.55% (10/1830).

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Authors' Contributions

B.W. led in the preparation of the manuscript, led the design and conduct of the quality improvement data query (preparatory to research), and analyzed all data. J.I. assisted in the preparation of the manuscript, reviewed the content of the quality improvement data

query (preparatory to research), and contributed text and context to the narrative. A.G. assisted in the preparation of the manuscript, performed a significant portion of the quality improvement data query, and contributed text and context to the narrative. M.M. assisted in the preparation of the manuscript, was central in the original quality improvement data query, and reviewed all data and text/context presented. All authors approved this manuscript.

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Manual of Operating Procedures (MOP) for 4-drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty Analgesia in Veterans

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Preface

This Manual of Operating Procedures is a guide for study staff conducting the “4-drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty Analgesia in Veterans Study” and is a supplement to the study protocol and should be used as a reference for the day-to-day conduct of the study. The success of the study depends on personnel cooperation and adherence to standardized procedures.

The MOP contains procedures for implementing: the study protocol; site management, recruitment and randomization; obtaining informed consent; collecting and reporting study data; and safety monitoring.

Contents

Preface	2
Introduction	6
STUDY TEAM ROLES AND RESPONSIBILITIES	7
Principal investigator (PI)	7
Co-Investigator (Co-I)	7
Study Coordinator (SC).....	8
Interdisciplinary Medical Preoperative Assessment Consultation and Treatment (IMPACT) CLINIC.....	9
Orthopedics.....	9
Investigational Drug Service (IDS)	9
Anesthesia service.....	10
Unblinded Mixers (MD or Certified Registered Nurse Anesthetists [CRNA])	10
Anesthesiologists.....	10
Physical therapy (PT)	10
University of Pittsburgh PT Staff	10
VA PT Staff.....	10
Regulatory specialist	11
Data manager and Statistician	11
SITE MANAGEMENT PROCEDURES	12
General Protocol Training	12
Protocol Amendment Training.....	12
Human Participants Training.....	12
Training Assignments	12
PROTOCOL PROCEDURES.....	13
Overview	13
Arm 1	13
Arm 2	13
Fixed dosing scheme for L2-L4 block.....	13
Fixed dosing scheme for L4-S3 block	13
Protocol for All Participants	13
Study Flowchart: Overall Study Progression	14
Procedures for Obtaining Consent and Screening	15

Recruitment and Pre-Screening Plan	15
Screening Using CPRS Notes	16
Patient ID Assignment at Time of Signed Consent.....	16
Procedures for Screening.....	16
Inclusion/Exclusion Criteria.....	16
Study ID Assignment and Randomization	17
Original block assignments.....	17
Procedures for randomization and SID assignment.....	18
Replacement Block Assignments	18
Randomization Envelope Handoff	19
Participant Status Terminology.....	19
STUDY VISIT MATERIALS AND ACTIVITIES	19
Screening Visit Assessments	19
Baseline Visit Assessments.....	20
Day of Surgery Assessments and Forms	20
Post Op Day 1 Assessments	20
Post Op Day 2 Assessments	21
Assessments for Post Op Day 3 to Day of Discharge	21
Week 2 Visit Assessments.....	22
Week 6 Visit Assessments.....	22
GOOD CLINICAL PRACTICES.....	23
Investigator Site File.....	23
Subject Study Binder	23
Source Documentation	23
Interactions with IRB and Research and Development (R&D) Committee.....	23
Archiving Study Records.....	23
STUDY MONITORING AND REPORTING	24
Pitt Education and Compliance Office for Human Subject Research.....	24
VAPHS Research Compliance Officer	24
Protocol deviations	25
Tracking protocol deviations.....	25
Notification of protocol deviations	25

Safety monitoring and reporting.....	25
Safety Reporting.....	26
Unblinding.....	26
ELECTRONIC DATA CAPTURE AND DATA MANAGEMENT.....	27
Data collection procedures.....	27
Data entry processes.....	27
Data verification process.....	27
Audit table in EDC	27
Data Backup processes.....	27
Data Analyses	27
Interim analyses	27
End of study analyses.....	27
Research publication.....	28
STUDY COMPLETION AND CLOSE OUT PROCEDURES.....	30
MISCELLANEOUS INFORMATION	31
Costs and payments	31
LIST OF APPENDICES.....	32

Introduction

After total joint replacement, early hospital discharge to home (with patients capable of continuing a home-based rehabilitation program) is a cost-effective management strategy. This project will use improved local anesthetic nerve block techniques to enhance technical capability and clinical practice by (i) reducing pain and other morbidities during recovery, (ii) improving weight-bearing achievement during in-hospital physical therapy to allow for earlier return home, and (iii) continued rehabilitation as an outpatient at home when feasible (versus in an extended care facility). The primary objective is to evaluate 3-day pain (recovery) and physical therapy (rehabilitation) outcomes based on bupivacaine MultiModal PeriNeural Analgesia (MMPNA) [i.e., bupivacaine-CBD (clonidine-buprenorphine-dexamethasone) versus plain bupivacaine for both L2-4 (0.2-0.25%) and L4-S3 (0.1-0.125%) blocks for joint replacement patients. Additional stratifications with regard to the blocks are age and diabetes. We currently anticipate 20 knee patients and 20 hip patients assigned to the active control group (bupivacaine without CBD) and 80 knee and 80 hip patients to the MMPNA treatment (bupivacaine with CBD).

STUDY TEAM ROLES AND RESPONSIBILITIES

Principal investigator (PI)

The PI is responsible for the management and scientific conduct of the study and must be familiar with the FDA guidance for PIs (Appendix 1), VHA Handbook 1200.05 (Appendix 2), local VA (IRB, Information Safety Office(r) [ISO], Privacy Office(r) [PO]), Department of Defense (DoD), and Pitt IRB. The PI or their designee will be responsible for:

- Completing all required training of researcher in the VA;
- Ensuring that the clinical investigation is conducted according to the investigational plan and applicable regulations;
- Being available to answer protocol or content-related questions;
- Protecting the rights, safety and welfare of participants under the investigator's care;
- Ensuring required trainings are completed by all study personnel;
- Delegating tasks to appropriately trained staff members, documenting on delegation log, and providing adequate supervision of those to whom tasks are delegated;
- All trial-related medical decisions and care;
- Routine meetings with staff to review trial progress, adverse events, protocol deviations, and changes to the protocol or other procedures;
- Procedure for the timely correction and documentation of problems and/or protocol deviations;
- Procedure for ensuring that the consent process is being conducted in accordance with 21 CFR Part 50 (Appendix 3) and that study participants understand the nature of their participation and the risks;
- Procedure for ensuring that source data are accurate, contemporaneous and original;
- Procedure for ensuring that information in source documents is accurately captured on the case report forms (CRFs);
- Procedure for dealing with data verification processes and data queries and discrepancies
- Determine whether Adverse Events (AEs) and Severe Adverse Events (SAEs) are related to study medications;
- Evaluate all protocol deviations and ensure necessary notifications are made;
- Procedures for ensuring study staff comply with the protocol and adverse event assessment and reporting requirements;
- Procedure for addressing medical and ethical issues that arise during the course of the study in a timely manner;
- Making the final decision regarding patient study participation;
- Administering anesthesia/study drug to patient; and
- Completing the Surgical Anesthesia and Recovery Room and Surgical Parameters forms;
- Support the Study Coordinator (SC) and engage with colleagues in an effort to identify potential study participants;
- Participate in all required audits.

Co-Investigator (Co-I)

- Function same as PI when PI is not available (see PI description above), except when function is outside their scope of practice; and

- Manage aspects of the study relevant to their areas of specialization.

Study Coordinator (SC)

The SC or their back-up will be responsible for:

- Identify and pre-screen potential participants from the Orthopedic Clinic to determine if they meet eligibility requirements;
- Provide the IMPACT Clinic Director of Medicine and Nurse Manager with a list of potential study participants;
- Communicate with Pitt PT Staff regarding the scheduling of potential study participants for Screening/Baseline visits;
- Explain the study to potential participants in a respectful, responsive, non-coercive manner in plain English;
- Review screening information with the PI/ Co-I prior to participant randomization;
- Conduct informed consent process;
- Provide the Cumulative Illness Rating Scale/Comorbidity (CIRS) to the IMPACT Clinic Director of Medicine once informed consent has been signed for completion;
- Assign each potential patient with a Patient Identification Number (PID) after signing of consent and a Study Identification Number (SID) at patient randomization;
- Provide study assignment to the Investigational Drug Service (IDS) staff using the Treatment Allocation Request Form (Appendix 4) (TARF) along with a copy of the signed Informed Consent;
- Fax copies of the signed Informed Consent Form (ICF) and HIPAA Authorizations to the VAPHS Research Compliance Officer (RCO) within 24 hours of signature;
- Ensure that the flagging mechanism (Research Study Alert) is in the participant's medical record in Computerized Patient Record System (CPRS);
- Administer study questionnaires (Appendix 5), Monday through Friday, as outlined in the study calendar (Appendix 6) prior to morning physical therapy visit;
- Maintain the PID and SID lists on a daily basis;
- Schedule Exam Room for Baseline and Week 6 study visits;
- Communicate with study and Social Work staff about patient discharge as outlined in the NERVE BLOCK Study Participant Post-Op Week 2 Ortho Clinic/Research Visit Social Work and Transportation Communication Procedure(Appendix 7);
- Schedule study participants for Weeks 2 and 6 follow-up visits as outlined in the NERVE BLOCK Study Participant Post-Op Weeks 2 AND 6 Ortho Clinic/Research Visit Scheduling Procedure(Appendix 8);
- Maintain the Nerve Block Calendar in Microsoft Outlook with scheduled patient visits and related communication as outlined in the Nerve Block Patient Information Communication and Study Form Distribution Procedures (Appendix 9);
- Coordinate with the Pitt PT Staff to ensure that all study related Physical Therapy evaluations are completed on the Clinical Exam Form (CEX);
- Remind patient of upcoming study visits;
- Provide primary point of contact for all participants in the study;
- Ensure all study records are complete and up-to-date, including the participant's study binder, consent forms, REDCap, Research Notes in CPRS and source documents;

- Ensure all protocol deviations and AE reports are appropriately documented;
- Enter questionnaire data into REDCap;
- Verify data entry completed by Pitt PTs;
- Maintain appropriate study documents in Nerve Block Share Drive;
- Share responsibility with StatCore for the development and maintenance of this study MOP.

Backup: Pitt PTs will serve as backup for completing the questionnaires during planned (scheduled) SC absences. The Clinical Trial Center (CTC) staff will be the backup for questionnaire administration and other coordination activities when absences are unexpected. New recruitment during SC's absence will be done by CTC or Pitt PT staff, as appropriate.

Interdisciplinary Medical Preoperative Assessment Consultation and Treatment (IMPACT) CLINIC

- SC will provide the IMPACT Clinic Medical Director and/or Nurse Manager with the names of potential participants;
- Ask the potential participant if s/he is interested in research opportunities;
- Advise the potential participant that there is a research study for which s/he may qualify;
- Ask the potential patient if a member of the study team may initiate contact via phone to discuss the study;
- Provide the SC with the names of interested potential participants;
- Complete and return the CIRS to the SC after informed consent has been signed.

Orthopedics

- Ask the potential participant if s/he is interested in research opportunities;
- Advise the potential participant that there is a research study for which s/he may qualify;
- Ask if a member of the study team may initiate contact via phone to discuss the study;
- Provide the SC with the names of potential participants; and
- Dictate 2 week and 6 week follow-up post-surgical visit dates.

Investigational Drug Service (IDS)

- Determine which of the treatment assignment number (1-5) corresponds to Control (bupivacaine only) versus Active (Bupivacaine plus CBD);
- Prepare the Nerve Block Preparation Instructions and Accountability form;
- Track the use of the nerve block drug mixing kits;
- Prepare and maintain control of Randomization Envelope (Nerve Block Preparation Instructions and Accountability form /Syringe Labels/Return Envelope) (Appendix 10);
- Ensure adequate supplies of nerve block drug components are stocked in the automated dispensing cabinet and refrigerator (clonidine syringe only);
- Provide Randomization Envelope containing the treatment allocation for the assigned randomization number to the PI/Co-I on the day before scheduled surgery (Friday for Monday surgery);
- Retrieve the SEALED return envelope containing the completed Nerve Block Preparation Instructions and Accountability form; and

- Verify completion of the form by the mixer and the treatment assignment noted on the form corresponds to the randomized treatment assignment noted on the Block Assignment sheet.

Anesthesia service

Unblinded Mixers (MD or Certified Registered Nurse Anesthetists [CRNA])

- Prepare the nerve block injection syringes based on the Randomization Envelope assignment;
- Hand the mixture off to a study team anesthesiologist;
- Complete the drug lot and expiration date on the Nerve Block Preparation Instructions and Accountability Form; and
- Make available to the PI or IDS the completed SEALED Randomization Envelope.

Anesthesiologists

- Receive Randomization Envelope from IDS;
- Assign Mixer to prepare nerve block; and
- Inject drug during surgery.

Physical therapy (PT)

University of Pittsburgh PT Staff

- Complete the ENTIRE Clinical Exam Form (CEX) form at the Baseline and Week 6 follow-up visits;
- Manage study visit forms by retrieving and returning the CEX form during daily assessments and treatments from/to locked file cabinet located in the second floor Physical Therapy office as described in the Nerve Block Patient Information Communication and Study Form Distribution Procedures;
- Perform standard of care (SOC) and Research treatment interventions during designated inpatient visits (Monday through Friday: Afternoon visits; Saturday and Sunday: Morning visits);
- Complete and record designated assessments on the CEX form during inpatient visits;
- Ensure CPRS is updated after each completed visit;
- Enter data into REDCap and select "Unverified" for form status when PT data entry is complete;
- Conduct informed consent process when SC is unavailable;
- Review screening information with the PI/Co-I prior to participant randomization;
- Administer study questionnaires per DoD protocol and as outlined in the study calendar when SC unavailable;
- Fax copies of the signed Informed Consent Form and HIPAA Authorizations to the VAPHS RCO when SC unavailable;
- Ensure that the flagging mechanism is in the participant's medical record in CPRS (Research Study Alert);
- Ensure all protocol deviations, AEs, and SAEs are communicated to SC as soon as possible and within IRB regulations;
- Maintain the Nerve Block Calendar in Outlook with scheduled patient visits;
- Communicate with SC about patient discharge;
- Communicate any missing data from VA PT CEX forms to VA Rehab Supervisor;
- Maintain the Physical Therapy Clinical Examination MOP (Appendix 11).

VA PT Staff

- Manage study visit forms by retrieving and returning the CEX form during daily assessments and treatments from/to locked file cabinet located in the second floor PT office as described in the Nerve Block Patient Information Communication and Study Form Distribution Procedures;
- Perform SOC treatment interventions during designated (Monday through Friday: Afternoon visits; Saturday and Sunday: Morning visits) inpatient visits;

- Complete and record designated assessments on the CEX form during inpatient visits; and
- Ensure CPRS is updated after each completed visit.

Regulatory specialist

- Serve as liaison between the PI, DOD, IRB(s) and FDA;
- Update Delegation Log to reflect personnel changes;
- Maintain Investigator Site File; and
- Complete all IRB and FDA submissions.

Data manager and Statistician

- Prepare Data Dictionary (REDCap);
- Develop and maintain CRFs;
- Verify data quality and validity;
- Manage, back-up, and store data;
- Share responsibility with the SC for the development and maintenance of the study MOP;
- Compile data for interim and final analysis and eventual dissemination of results to provider meetings, professional conferences and peer reviewed journals.

SITE MANAGEMENT PROCEDURES

General Protocol Training

Prior to starting any study activities, the study team conducted a Site Initiation Visit (SIV). All study team members were invited and trained on the protocol. The meeting included: protocol review and detailed discussion of study implementation; MOP/study procedures review; CRF completion; data collection; investigational product distribution and handling; safety reporting; clinical monitoring; good clinical practice; study staff responsibilities; and record retention. The SC created a PowerPoint presentation for use during the session. Any team member who was unable to attend was emailed the slides for their review and documentation of study training. Additional training will be provided as needed.

Protocol Amendment Training

Each time a substantial amendment is submitted and IRB approved, the SC will create an updated presentation detailing relevant protocol changes. These training slides will be emailed to the study team for review and acknowledgement. For each completed training session, study staff training will be documented on the site training log which will be kept in the Regulatory Binder.

Human Participants Training

All members of the research team listed on the IRB application as non-exempt staff will be required to complete human participant research training prior to starting study activities and every three years while participating in this research study. Human participant training certificates will be maintained in the Regulatory Binder.

Training Assignments

- o REDCap training for all data entry personnel done by StatCore
- o VA PT training Pitt PT on CPRS entries and VA PT protocols
- o Research Office administration to oversee and verify necessary VA online (TMS) and Human Subjects/Good Clinical Practice (CITI) trainings for all study staff.
- o CTC backup staff for research protocol training done by SC
- o Questionnaire training done with Pitt PTs by SC
- o Anesthesiologist/Mixer training done by PI and/or by IDS pharmacist
- o Pitt PT to train VA PT staff on the CEX

PROTOCOL PROCEDURES

Overview

Multimodal systemic analgesia (oral and intravenous, with mechanisms involving those other than nerve block analgesia) will be standardized and provided for all patients consistent with our routine clinical practice. Patients undergoing primary hip or knee replacement surgeries will be randomly assigned to one of two single-injection nerve block drug treatments: Plain bupivacaine (“active control”) or MMPNA. The bupivacaine dose will be based on the patient’s diabetic status as determined during the patient’s SOC screening for surgery.

Arm 1

Patients in the plain bupivacaine group (“Active Control”) will receive L2-L4 and L4-S3 nerve blocks plus standardized spinal anesthetic

Arm 2

Patients in the MMPNA group will receive bupivacaine-clonidine-buprenorphine-dexamethasone (Bupivacaine-CBD) plus standardized spinal anesthetic

Fixed dosing scheme for L2-L4 block

Diabetics will receive one 20 mL syringe that will contain 8 mL 0.5% bupivacaine and either 12 mL Preservative Free Normal Saline (PFNS) or 10.65 mL PFNS plus 300mcg/1ml buprenorphine, 25 mcg/0.25mL clonidine, and 1mg/0.1mL preservative-free dexamethasone sodium phosphate. The net concentration of bupivacaine will be 0.2%.

Non-diabetics will receive one 20 mL syringe that will contain 10 mL 0.5% bupivacaine with either 10 mL PFNS or 8.65 mL PFNS plus 300mcg/1mL buprenorphine, 25 mcg/0.25mL clonidine, and 1mg/0.1mL preservative-free dexamethasone sodium phosphate. The net concentration of bupivacaine will be 0.25%.

Fixed dosing scheme for L4-S3 block

Irrespective of diabetes, patients will receive 4 mL 0.25% bupivacaine, plus 14.65 or 16 mL PFNS. If only 14.65 mL PFNS, then also 300mcg/1ml buprenorphine, and 25 mcg/0.25mL clonidine, and 1mg/0.1mL preservative-free dexamethasone sodium phosphate. The net concentration of bupivacaine will be 0.1%.

Protocol for All Participants

All patients will receive a standardized bupivacaine spinal anesthetic, consistent with current institutional practice. All patients will receive pre-medications for the prevention of pain, nausea, vomiting, and gastroesophageal reflux, consistent with current institutional practice. All patients will receive intravenous hydration, intravenous antiemetics, and intravenous blood pressure support (e.g., intravenous phenylephrine bolus/infusion) consistent with our current institutional practice. The need for intraoperative blood transfusion will occur based on current institutional practice and collaborative decision-making between the surgical and anesthesia teams, consistent with current institutional practice. Participant involvement in this study will be approximately 3 to 4 months after signing Informed Consent.

Study Flowchart: Overall Study Progression



Procedures for Obtaining Consent and Screening

Recruitment and Pre-Screening Plan

The HIPAA Waiver obtained by the Regulatory Specialist and approved by the VAPHS IRB allows the Study Staff to access and use patient medical record information for pre-screening purposes. The study team (typically the SC) will prescreen the medical records of patients scheduled to be seen in the orthopedic clinic via CPRS record review. When the SC finds a potentially eligible patient, the SC will advise a member of the patient's clinical care team, specifically a member of the orthopedics/surgical team or IMPACT clinic team. The patient will then be approached by a member of their clinical care team to see if they are interested in participating in research opportunities. If the patient expresses interest, the study team will be notified via a phone call or encrypted email.

Once notified, the study team will either provide the potential participant with the ICF to take home or send it to them via US Mail (Appendix 12) in order to give them time to review on their own or with family/friends. The study team will let the patient know that s/he can call at any time with questions to help aid in the decision, and that the study team will be calling the patient in a few days after s/he has had time to review the ICF, and/or to declare interest and/or ask questions. Additional information about the study may be provided to the patient but no substantive addition, deletion or modification of the approved ICF is permitted. If the patient is interested, the study team will schedule the potential participant for their Screening/Baseline visit, at which time ICF completion will occur.

If the patient is scheduled for an eConsult IMPACT clinic visit, the study team will schedule the potential participant to come in for a research only Screening/Baseline visit. If the potential participant is already scheduled for a face-to-face IMPACT clinic visit, the study team will ask the patient if they wish to complete the Screening/Baseline visit on the same day or if they would prefer to schedule a separate visit, as the Screening Baseline visit is expected to take approximately three (3) hours. When scheduling for this visit, Study Staff will advise the potential participant to wear comfortable clothing and shoes, bring their glasses and wear their hearing aids, if necessary.

The consent process will occur either in an empty room, or, if necessary, in an exam room where a curtain will be drawn and the discussion will be kept quiet to ensure patient confidentiality. Once the consent is signed, one of the physician-investigators will make the final determination of eligibility of potential participants. A potential participant can sign the consent form but the potential participant may be declared ineligible after physician review.

Informed consent requires that the participant understands the details of the study and agrees, without coercion, to participate. In conjunction with the ICF, the potential participant will be asked to review and sign the Authorization for Use and Release of Individually Identifiable Health Information Collected for VHA Research Form as required by HIPAA.

The most current approved version of the ICF will be available on the CTC-approved shared drive and will be updated every time a new version is approved. When obtaining consent, the header of each page must include

the participant's name, the date the ICF was signed, both the participant's and the Study Staff's printed name and signature as well as the time signed. If the patient chooses not to sign consent, no research procedures will be completed.

Once the consent is signed, copies are distributed as follows:

- o Original to SC for placement in patient's study binder
- o Copy to patient
- o Copy to VAPHS RCO either by fax (22-1569) or by interoffice mail using a VHA Internal Privacy Act/HIPAA envelope to Research Compliance 131-A
- o Copy from SC to IDS with TARF (paper copy)

The flowchart of the process "From Prescreening to Obtaining Informed Consent" is located in Appendix 13.

Screening Using CPRS Notes

The participant's CPRS chart must be updated after each research study visit after the patient has signed consent. Notes will be entered using established templates (Appendix 14), as follows:

- Screening/Baseline Visit
 - o Research Study Alert
 - o Research Initial Consent Note
 - o Research Note
- All other research study visits
 - o Research Note

Every attempt will be made to schedule the Screening and Baseline Visits on the same day. Should these Visits be conducted on separate days, the Research Study Alert and Research Initial Consent Notes need only be entered at the Screening Visit.

Patient ID Assignment at Time of Signed Consent

The SC will assign each potential participant a Patient ID number (PID – [NBxxx]) at the time of signed consent in order to track all consented patients regardless of eligibility. If deemed eligible, participants are assigned a Study ID (SID) number which corresponds with their Randomization Envelope. Participant charts will be identified by SID number.

Procedures for Screening

Inclusion/Exclusion Criteria

Inclusion Criteria

Subjects must meet all of the following inclusion criteria to be eligible for participation in this study.

1. Age between 18 and 85, and undergoing a total knee or hip replacement.
2. Fluent in English, decision competent, willing and able to provide written informed consent, and able to complete the study's schedule of assessments.
3. Able to walk >3m without an assisting device.

4. Have a BMI $\leq$ 40 kg/m².

Exclusion Criteria

Subjects who meet *any* of the following exclusion criteria will not be enrolled in this study.

1. Current participation in another orthopedic/PT/rehab/anesthesiology interventional clinical trial.
2. Are at significant behavioral risks or have refractory major psychiatric disorders.
3. Revision surgery on the same extremity.
4. Have an ASA Physical Status classification of 4 or higher.
5. Have been diagnosed with clinically significant neuropathy with its origins in either diabetes or other causes; have neuromuscular disease that would influence data collection.
6. Have a surgically-fused lumbar spine, or a spinal cord simulator, or other condition that would contraindicate or prohibit the conduct of spinal anesthesia.
7. At significant risk for postoperative substance abuse, or immediate-postoperative substance abuse withdrawal symptoms (alcohol, cocaine, enrolled in methadone or buprenorphine opioid withdrawal programs, etc.)
8. Are undergoing TKA/THA for a tumor.
9. Have contraindications (e.g., anaphylaxis) to any of the study drugs.
10. Have a systemic fungal infection.
11. Have a known hypersensitivity to bupivacaine hydrochloride or to any local anesthetic of the amide-type or to other components of bupivacaine hydrochloride solutions.
12. Have a known or suspected buprenorphine hypersensitivity (not including nausea and/or vomiting).
13. Have a GI obstruction.
14. Have paralytic ileus.
15. Pregnant women

Pregnancy is an exclusion criterion for surgery and a pregnancy test will be done by the clinical team on the day of surgery in appropriate participants. The Research team will confirm that the pregnancy test has been done (where applicable).

Study ID Assignment and Randomization

Original block assignments

Pre-established unique study IDs (SIDs) will be assigned as participants are deemed eligible and randomized. SIDs were created with up to four replacements per block, where block assignment is based upon surgery location, diabetes status, and age. Meaning that in the event that a block-assigned participant cannot complete the protocol after the SID has been assigned, additional SIDs have been created to allow 4 replacement block-specific SIDs. Files that list SIDs are available in the study's shared drive at [\\r04pthnas21.v04.med.va.gov\PTH_Groups\Nerve_Block_Study](\\r04pthnas21.v04.med.va.gov\PTH_Groups\Nerve_Block_Study). A hard copy of the assigned and available SIDs will be updated and maintained by the SC in a recruitment binder.

The flowchart related to the process "From Consented to Enrolled" is located in Appendix 13.

SIDs were created using an 8-digit number system consisting of the following:

Section	Values
Surgery Type	1 = TKA, 2 = THA
Diabetes presence	0 = Absent, 1 = Present
Age classification	6 = ≤69yo, 7 = >69yo
Drug assignment	1 through 5
4 digit enrollment #	1001 through 9999

For example, the first subject that is getting TKA, diabetes is absent, and is aged ≤ 69 has received the Subject ID 10651001. This scheme creates the following block assignment sections, as follows:

Subject characteristics	First 3 values of Participant ID
Total knee replacement, Diabetes absent, aged ≤ 69	106
Total knee replacement, Diabetes absent, aged > 69	107
Total knee replacement, Diabetes present, aged ≤ 69	116
Total knee replacement, Diabetes present, aged > 69	117
Total hip replacement, Diabetes absent, aged ≤ 69	206
Total hip replacement, Diabetes absent, aged > 69	207
Total hip replacement, Diabetes present, aged ≤ 69	216
Total hip replacement, Diabetes present, aged > 69	217

Procedures for randomization and SID assignment

- Prior to the DOS, the SC will submit a Treatment Allocation Request Form (TARF) to the IDS Pharmacist, along with a copy of the signed ICF
- The TARF will indicate the subject's criteria:
 - Age: ≤69 or >69 years
 - Type of procedure: total knee replacement or total hip replacement
 - Diabetes status: present or absent
- Based on the criteria, the IDS Pharmacist will provide the next available Randomization Envelope which corresponds with their SID number.

Replacement Block Assignments

Study drug assignment and subject numbering will occur in sequential order that is described in the Block Assignment and Subject Numbering schedule under the Original heading. This schedule consists of eight sections that cover the subjects procedure (TKA or THA), diabetes presence (present or absent), and age (69 or younger, older than 69). For example, in Total Knee Replacement, Diabetes Absent, aged ≤ 69, the first subject will receive number 10651001 and block 1 drug #5, the second subject will receive number 10641002 and drug #4, and so forth. This will proceed sequentially until all planned drug and numbering assignments are completed. The subjects will be tracked until study completion. If a subject does not complete the study, their drug assignment will be replaced with a corresponding drug assignment and new subject number from Replacement #1 schedule; if the replacement subject fails to complete the next subject will receive the corresponding drug assignment and subject number from Replacement #2 schedule, and so forth.

Randomization Envelope Handoff

- Distribution will occur on the day prior to Day of Surgery (DOS) or on Friday for Monday surgeries
- IDS gives Randomization Envelope to PI/Co-I one day prior to DOS
- PI/Co-I gives Randomization Envelope to Anesthesia Mixer on DOS
- Anesthesia Mixer will open the randomization envelope to retrieve the form indicating the treatment assignment and document preparation and accountability on DOS
- The Mixer will place the randomization envelope and completed preparation and accountability form in a provided return envelope that will be sealed and returned to IDS for safe-keeping.

The process flowchart “From Enrolled to Randomization Envelope Handoff” is located in Appendix 13.

The process flowchart “From Randomization Envelope Handoff to Anesthesia Preparation” is located in Appendix 13.

Participant Status Terminology

Participants going through study visits will be classified and reported on by the following study status terms.

Screened: Completion of all screening processes to determine eligibility.

Consented/Enrolled: Prior to any study activities and may occur before or at the Screening/Baseline visit, and is concurrent with both enrollment and assignment of the Participant ID (PID) number. Once they have consented they are considered enrolled.

Screen failure: Determined at Screening/Baseline visit and based on presence of exclusion criteria and/or physician judgement

Eligible: Determined as eligible after review of inclusion/exclusion criteria during screening process

Randomized: Occurs after deemed eligible and when SC assigns SID. SID functions as randomization assignment.

Active in follow-up: Any participant active in study after surgery.

Completed: Completion of week 6 follow-up visit

Early Termination: Occurs after the participant has been enrolled and is initiated by either the PI/Co-I or participant

Withdrew consent: Occurs any time after the patient has been consented and has decided not to further participate in the study

Lost to follow-up: Any participant who has become unreachable during the follow-up period of the study (Post Op Day through Week 6 Visit). Study Staff is to make 3 attempts to contact patient over 3 weeks after their last missed visit.

STUDY VISIT MATERIALS AND ACTIVITIES

Screening Visit Assessments

- Consent Verification (CONS)
- Eligibility (EL)
- Demographics (DEMO)

Baseline Visit Assessments

- Western Ontario & McMaster Universities Osteoarthritis Index (WOMAC)
- Short-Form McGill Pain Questionnaire 2 (SFMPQ2)
- Defense and Veterans Pain Rating Scale (DVPRS)
- Opioid-Related Symptom Distress Scale (ORSDS)
- Quality of Recovery (QOR15)
- SF-36 Health Survey Version 2 (SF36V2)
- Cumulative Illness Rating Scale/Comorbidity (CIRS)
- Falls – Pre
- Clinical Exam Form (CEX) – Complete
 - Straight Leg Raise
 - Range of Motion (ROM)
 - Sensation/Light Touch
 - Functional Independence Measure (FIM) for Transfers, Locomotion, and Stairs
 - Standing Balance Tests
 - Gait Speed
 - Repeated Chair Stand Test
 - Stair Climbing Test
 - Single-Leg Balance Test

Day of Surgery Assessments and Forms

Prior to Surgery

- SF-8 Health Survey 24 Hour Recall Version (SF8)
- SFMPQ2
- DVPRS

Post-Surgery/Recovery

- SFMPQ2
- DVPRS

Surgery Information Forms

- Surgical Parameters
- Surgical Anesthesia and Recovery Room

Post Op Day 1 Assessments

Prior to Morning PT Session

- SFMPQ2
- SF8
- QOR15
- ORSDS
- Defense and Veterans Pain Rating Scale – In Hospital (DVPRS – IH)

Morning and Afternoon PT Sessions

- CEX – Selected Sections
 - Straight Leg Raise
 - Range of Motion (ROM)
 - Sensation/Light Touch
 - FIM for Transfers, Locomotion, and Stairs
 - Standing Balance Tests
 - Gait Speed
 - Therapeutic Exercise
 - Pain Assessment

Post Op Day 2 Assessments

Prior to Morning PT Session

- SFMPQ2
- SF8
- QOR15
- ORSDS
- DVPRS – IH

Morning and Afternoon PT Sessions

- CEX – Selected Sections
 - Straight Leg Raise
 - Range of Motion (ROM)
 - Sensation/Light Touch
 - FIM for Transfers, Locomotion, and Stairs
 - Standing Balance Tests
 - Gait Speed
 - Repeated Chair Stand Test
 - Therapeutic Exercise
 - Pain Assessment

Assessments for Post Op Day 3 to Day of Discharge

Prior to Morning PT Session

- SFMPQ2
- SF8
- QOR15
- ORSDS
- DVPRS – IH

Morning and Afternoon PT Sessions

- CEX – Selected Sections
 - Straight Leg Raise
 - Range of Motion (ROM)

- o Sensation/Light Touch
- o FIM for Transfers, Locomotion, and Stairs
- o Standing Balance Tests
- o Gait Speed
- o Repeated Chair Stand Test
- o Therapeutic Exercise
- o Pain Assessment

Week 2 Visit Assessments

- DVPRS
- SF8

Week 6 Visit Assessments

- WOMAC
- SFMPQ2
- DVPRS
- SF36V2
- CEX – Complete
- Falls – Post
- Interim Changes in Signs & Symptoms (ICHG)
- Discharge Disposition & Rehabilitation (DCR)

Concomitant medications (Con Meds), SAEs and AEs logs are collected at every visit after screening. Data will be collected on paper (source document) during each visit and entered into the REDCap electronic database after visit completion. For additional details about the EDC process, go to the section entitled “Data Collection Procedures.”

GOOD CLINICAL PRACTICES

This trial will be conducted in compliance with Good Clinical Practice (GCP) regulations. The intent of these regulations is to safeguard subjects' welfare and assure the validity of data resulting from the clinical research.

Investigator Site File

The regulatory coordinator for the study will be responsible for maintaining all investigator site files and preparing them for monitoring visits and audits and making it readily available to all study personnel. The binder will be updated throughout the course of the trial. The investigator site file will be kept in a secure environment.

Subject Study Binder

GCP requires that sites keep adequate and accurate case histories for study subjects. To comply with this requirement, the SC will be responsible for establishing and maintaining a Subject Study Binder for each study participant. The Subject Study Binder consists of all documents related to a specific individual's participation in the trial. This file will hold the original signed ICF, CRFs and source documents generated during the course of the trial.

Source Documentation

Source documentation must be maintained to ensure integrity of the study data. Source documentation is defined as the original initial recording of the study information. The Subject Study Binder will contain the source documents for the data recorded on the case report forms (CRF) and CPRS chart notes. This practice helps ensure compliance with the requirement that supporting documents be readily identifiable and accessible.

Interactions with IRB and Research and Development (R&D) Committee

This study is utilizing the VAPHS IRB and the University of Pittsburgh IRB. It is the regulatory coordinator's responsibility to ensure that the protocol is approved by both IRBs and the local VA R&D committee. The VA Assistant Chief of Staff (ACOS) for R&D is responsible for notifying the investigator when a research project can be initiated. This notification occurs only after the research project has been approved by all applicable R&D Committee subcommittees and after the R&D subcommittee's notifications of approval have been approved by the R&D Committee.

Archiving Study Records

All research records will be maintained in accordance with the Veterans Health Administration (VHA) Records Control Schedule. Paper records will be disposed of using methods deemed appropriate by the VAPHS PO, and all electronic data will be sanitized using methods rendered appropriate by the VAPHS ISO.

STUDY MONITORING AND REPORTING

Pitt Education and Compliance Office for Human Subject Research

The University of Pittsburgh's Education and Compliance Office for Human Subject Research (ECO-HSR) will monitor this research study. A study team member will contact the ECO-HSR staff whenever the first subject is scheduled and then initiate enrollment updates on at least a monthly basis.

The ECO-HSR staff will schedule an interim monitoring visit after the first enrolled subject undergoes the surgery and postoperative hospital stay associated with the study. All acknowledge that there may be more than one study patient undergoing surgery on a given day, so there may be more than one enrolled subject having completed surgery and the hospital stay by the time the ECO-HSR staff makes its interim monitoring visit. The frequency for subsequent interim monitoring visits will be based on factors such as enrollment, significant changes in study design or status, notable adverse or reportable events, etc.

For each monitoring visit the ECO-HSR staff will email the study team to confirm a visit date and provide a visit agenda. A study team member will be available on the day of the visit to facilitate monitoring activities. An exit interview to review monitoring visit findings will be conducted as warranted with the investigator after the completion of a monitoring visit.

The ECO-HSR staff will review, as applicable, the original source documents for at least 20% of enrolled subjects at each visit to ensure adherence to the FDA protocol and the evaluation, follow-up, and reporting of adverse events. The VAPHS RCO will audit 100% of VA informed consents per VAPHS policy. ECO-HSR review of consent documents will be limited in scope and may include those associated with subject records reviewed for the purpose of the monitoring visit or others as deemed necessary.

The regulatory file will be reviewed at each interim monitoring visit, as time permits.

The ECO-HSR staff will generate a monitoring visit report. Action items resulting from the visit will be identified in the report and assigned to a member of the study team. The ECO-HSR staff will verify completion of the action items.

Monitoring visit reports, reportable events associated with the visit, and/or any other applicable documents will be reviewed by the Compliance Activity Review Subcommittee (CARS). The CARS is comprised of the following University of Pittsburgh representatives: IRB Chair, IRB Regulatory Affairs Specialist, O3IS Director, ECO-HSR Director, ECO-HSR Medical Monitor, and ECO-HSR Staff. The CARS will determine whether issues warrant review by the IRB Executive Committee.

VAPHS Research Compliance Officer

The VAPHS Research Compliance Officer (RCO) will conduct triennial audits during the life of the research study. Audits may include an interview with the PI and/or key study personnel, such as the SC, regarding recruitment and enrollment procedures, the informed consent process, staff training and responsibilities, IRB procedures, and data and safety monitoring. During the audit a random sample of study subject files and

consent forms will be reviewed for adherence to the IRB-approved protocol and appropriate documentation of informed consent.

All active human research studies must receive an informed consent audit, whether or not any informed consent documents were required or signed. At VAPHS, once a study has begun recruiting, the study team must submit a copy of each signed informed consent document to the VAPHS RCO within 1 business day of the subject's signature. The VAPHS RCO will review each consent form received to ensure compliance with applicable regulations and policies related to informed consent.

A regulatory audit will also be conducted.

At the conclusion of the audit, an audit report will be prepared by the VAPHS RCO. A copy of the audit report will be provided to the PI and to the VAPHS IRB.

Protocol deviations

Protocol deviations include, but are not restricted to, the following:

- Randomization of an ineligible participant;
- Failure to obtain informed consent;
- Failure to keep IRB approval up to date; and
- Wrong treatment administered to participant.

Protocol deviation logs will be tracked along with SAE and AE logs and submitted to IRB as necessary.

Tracking protocol deviations

The protocol deviations will be noted on the Protocol Deviation Log and will be reported to the IRBs, DSMB, and FDA (as indicated) at each reporting period, via this log.

Notification of protocol deviations

All deviations, as soon as noted, should be reported to the principal investigator within 24 hours of occurrence or discovery. Routing of notification of these deviations will be determined by the PI.

Safety monitoring and reporting

AEs are not reported to IRB, but are communicated to SC for logging. SAEs are communicated to SC and PI as soon as possible for regulatory personnel review and potential reporting to IRB. A listing of reportable events is available from the VAPHS IRB as a reference to all research staff. (Appendix 15)

The PI/Co-I and the SC are the points of contact for all SAE reporting. VA IRB requires the reporting of unexpected SAEs within 5 days of discovery. Regulatory personnel will also report SAEs to FDA and DoD monitoring boards.

All falls will be documented in the patient chart. If the fall is determined to be an SAE, it will be reported to the appropriate regulatory authorities as per current guidelines

Safety Reporting

A local data and safety monitoring plan has been implemented to ensure that there are no changes in the benefit/risk ratio during the study and that confidentiality of research data is maintained. It will meet as needed to discuss the study (e.g., study goals, progress, modifications, documentation, recruitment, retention, data analysis and confidentiality) and address any issues or concerns. The PI and relevant research staff will take part in these discussions. These will occur on an as needed basis and officially every six months. Any instances of adverse events, protocol deviations, or other problems identified during the discussions will be reported as soon as possible within the required reporting timeframes using the standard forms and/or procedures set forth by the IRB and/or monitoring body. Meeting minutes will be kept.

As with any standard of care surgical procedure, standard of care anesthetic procedure, or experimental procedure, there may be adverse events or side effects that are currently unknown, and such unknown risks could be permanent, severe, and/or life-threatening.

All adverse events and severe adverse events will be reported to the IRBs (VA and Pitt), DSMB (Pitt), and the Food and Drug Administration (FDA, related to this study involving an IND) using the formats and timelines directed by each of these regulatory bodies.

Unblinding

This is a double-blind study. Under non-SAE circumstances, neither the subject nor any member of the study team will know which of the two treatments the subject is receiving. Only the Mixer and IDS staff will know the treatment assignment. The PI or Co-I may request that a subject's treatment assignment is unblinded only in the event of an emergency or a serious medical condition and/or when knowledge of the study treatment is essential for the appropriate clinical management or welfare of the subject, as judged by the PI, Co-I or treating physician. The PI or Co-I will have access to the subject's study treatment assignment by contacting IDS during office hours or the VAPHS Inpatient Pharmacy during off hours. A copy of the completed Nerve Block Preparation Instruction and Accountability Form identifying the subject's treatment assignment will be given to the PI, Co-I and/or the SC in accordance with local and FDA regulations.

The date and reason for the unblinding must be fully documented in the appropriate data collection tool. Treatment codes will not be broken for the planned analyses of data until all decisions on the evaluability of the data from each individual patient have been made and documented. The number of individuals at the study site who become aware of the treatment status should be kept to an absolute minimum including keeping the patient blinded if possible.

ELECTRONIC DATA CAPTURE AND DATA MANAGEMENT

Data will be initially captured on paper forms for all the study questionnaires. These paper questionnaires will be considered the study's source documents and will be used to populate REDCap, an electronic data capture (EDC) and storage program approved for VA studies. The data will be entered into REDCap by either the Pitt PTs or the SC based upon assigned responsibility. Once entered, data will be verified by either the SC or StatCore based upon assigned responsibility and using the source documents as the basis for verification.

Data collection procedures

Data entry processes

Data entry into REDCap will be completed by either the SC or the Pitt PTs. All participants will be easily viewable from the REDCap interface in a tabular format by the presence of green (complete), yellow (unverified), and red (incomplete) symbols specific to participant, questionnaire, and visit.

Data verification process

Data verification will occur in 100% of data captured. The SC will verify data entered by the Pitt PTs. StatCore will verify the data entered by the SC. Whoever verifies the data in REDCap will complete and lock the record from further data entry. If a discrepancy is found in the data, the reviewer will create a query in REDCap which will need to be addressed. Once the query has been addressed it can be resolved and the data can be locked. Data requiring edits after record locking will be done by StatCore directly within the data table with audit notation of modification, date/time of change, and initials of person making modification.

Audit table in EDC

REDCap has an audit table function that tracks the changes made prior to record completion. Alterations tracked include when and by whom the alterations were made to data.

Data Backup processes

Data will be backed-up by StatCore on a weekly basis as an Excel worksheet exported from REDCap and saved in a restricted shared drive that only StatCore can access. A minimum of four weeks' worth of files will be saved at a time.

Data Analyses

StatCore will provide data summarizations as requested by the Institutional Data Safety Monitoring Board (IDSMB). Specifically, results presented will include adverse events, protocol deviations, and enrollment summary tables for overall primary and secondary endpoints per the IDSMB Excel-based reporting template. IDSMB meetings will occur as per IDSMB charter.

Interim analyses

StatCore will work with the IDSMB board to complete an interim analysis as per the IDSMB charter.

End of study analyses

The primary hypothesis of an improvement in pain (measured by the SF-MPQ- version 2) 24 hours after surgery during in-hospital recovery comparing plain local anesthetics versus ISOC MMPNA will be tested using

a mixed model. This procedure will test for nerve block drug treatment and surgical site (hip versus knee) effects, as well as an interaction between them. Data will first be assessed for outliers (± 2 SD from the mean) and normality. Outliers will be corrected, if possible, or dropped from the analyses. Distribution, measures of central tendency, variability, and normality will be examined. Data transformations or non-parametric techniques will be applied as needed. We will delete observations with missing values. Spearman's correlation coefficients will be computed to examine associations between nerve block drug treatments, replacement surgery type (hip versus knee), and the outcome measures from all time points (1 day, 2 day, 3 day, 4 day, 2 week, 6 week). Associations between the outcomes across time points will also be examined with Pearson and Spearman correlation coefficients, as appropriate. We will test all hypotheses and aims by conducting longitudinal multi-level modeling. The level-one unit will be the repeated measures across time, the level-two unit will be the individual patient, and the level-three unit will be nerve block type and surgical site (knee versus hip) groupings (with additional analyses involving age and diabetes status, reflecting the randomization strata). This mixed model procedure will allow the assessment of outcome and exposure variables relationships while adjusting for covariates, and separate assessments of fixed (group) and random (individual level) effects using highly correlated repeated measures data. Covariates included in modeling will be age, diabetes status, gender, weight, smoking status, initial health status, and concurrent general health status.

Research publication

For peer-reviewed manuscript submission regarding study proceedings submitted to journals of anesthesiology, pain, general medicine, or public health/epidemiology, the PI will determine study team co-author membership and author listing sequence (versus acknowledgment status without authorship). For peer-reviewed manuscript submission regarding study proceedings submitted to journals of orthopaedic surgery, physical therapy/rehabilitation/physiatry, or rheumatology, lead co-investigator Dr. Sara Piva will determine study team co-author membership and author listing sequence (versus acknowledgment status without authorship). It is anticipated that all submitted peer-reviewed publications will entail sufficiently active authorship roles by Drs. Williams and Piva that both will be listed on most if not all such submissions. Exceptions to this may (but not necessarily) include editorials, letters to the editor, or other "special correspondence" categories that do not fit the typical definition of "original research." Any special cases that deviate from these concepts will be determined privately between Drs. Williams and Piva on a case by case basis. If Drs. Williams and Piva are unable to reach mutual consensus in general or on special cases regarding such issues, they will consult with the VAPHS ACOS of R&D, first for guidance, and subsequently for adjudication if unable to reach consensus after guidance. If either Dr. Williams or Dr. Piva wishes to appeal the adjudication decision of the VAPHS ACOS R&D, then they can consult with the University of Pittsburgh Institutional Data Safety and Monitoring Board, the consultation of which will likely generate a fee.

If Pitt IDSMB judgment reverses the adjudication of the VAPHS ACOS R&D, then one-third of the DSMB fee will be covered by the party initiating the IDSMB appeal, with the other party covering the remaining two-thirds of the IDSMB fee.

If Pitt IDSMB judgment upholds the adjudication of the VAPHS ACOS R&D, then two-thirds of the DSMB fee will be covered by the party initiating the IDSMB appeal, with the other party covering the remaining one-third of the IDSMB fee.

At present, DSMB meeting fees are approximately \$500-700 to conduct a meeting.

STUDY COMPLETION AND CLOSE OUT PROCEDURES

- Verification that study procedures have been completed, data have been collected and study drugs and supplies have been returned to the VAPHS Pharmacy supply
- Assurance that all data queries have been completed
- Assurance that correspondence and study files are accessible for external audit
- Assurance that the investigator notifies the appropriate administrative entities of study completion and obtains a copy of the notification
- Performance of a Close-Out Monitoring Visit by ECO-HSR

MISCELLANEOUS INFORMATION

Costs and payments

Study participants will not be charged for any costs related to research.

Study participants will receive compensation for participating in this study. Study participants will receive a Greenphire ClinCard MasterCard Debit Card which will be activated by the SC after completion of the Baseline Visit. Patients will be compensated as follows:

- \$20.00 – Completion of Baseline Visit (Pre-Surgery Questionnaires and Physical Therapy Tests)

- \$20.00 – Completion of In-Hospital Questionnaires and Physical Therapy Tests

- \$60.00 – Completion of Week 6 Questionnaires and Physical Therapy Tests

LIST OF APPENDICES

APPENDIX 1.	FDA Guidance for PIs
APPENDIX 2.	VHA Handbook 1200.05
APPENDIX 3.	21 CFR Part 50
APPENDIX 4.	Treatment Allocation Request Form (TARF)
APPENDIX 5.	Visit Materials - Study Questionnaires, Forms and Logs
APPENDIX 6.	Study Calendar
APPENDIX 7.	NERVE BLOCK Study Participant Post-Op Week 2 Ortho Clinic/Research Visit Social Work and Transportation Communication
APPENDIX 8.	NERVE BLOCK Study Participant Post-Op Weeks 2 AND 6 Ortho Clinic/Research Visit Scheduling
APPENDIX 9.	NERVE BLOCK Patient Information Communication and Study Form Distribution Procedures
APPENDIX 10.	Randomization Envelope Example and Contents
APPENDIX 11.	Pitt Physical Therapy Clinical Examination MOP
APPENDIX 12.	Patient Consent Letter
APPENDIX 13.	Process Flowcharts
APPENDIX 14.	CPRS – Chart Note Templates and Entry Instructions
APPENDIX 15.	VAPHS Human Subjects Research List of Reportable Events
APPENDIX 16.	List of Acronyms
APPENDIX 17.	Nerve Block Study MOP Change Log

Guidance for Industry

Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)**

**Procedural
October 2009**

Guidance for Industry Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects

*Additional copies are available from:
Office of Training and Communication
Division of Drug Information, HFD-240
Center for Drug Evaluation and Research
Food and Drug Administration
(Tel) 301-827-4573
<http://www.fda.gov/cder/guidance/index.htm>*

or

*Office of Communication, Training and
Manufacturers Assistance, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
<http://www.fda.gov/cber/guidelines.htm>.
(Tel) 800-835-4709 or 301-827-1800*

or

*Office of Health and Industry Programs
Division of Small Manufacturers, International, and Consumer Assistance, HFZ-220
Center for Devices and Radiological Health
Food and Drug Administration
Tel: 1-800-638-2041
www.fda.gov/cdrh*

**U.S. Department of Health and Human Services
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October 2009**

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TABLE OF CONTENTS

I.	INTRODUCTION.....	1
II.	OVERVIEW OF INVESTIGATOR RESPONSIBILITIES	1
III.	CLARIFICATION OF CERTAIN INVESTIGATOR RESPONSIBILITIES	2
A.	SUPERVISION OF THE CONDUCT OF A CLINICAL INVESTIGATION	2
1.	<i>What Is Appropriate Delegation of Study-Related Tasks?</i>	<i>3</i>
2.	<i>What Is Adequate Training?.....</i>	<i>4</i>
3.	<i>What Is Adequate Supervision of the Conduct of an Ongoing Clinical Trial?.....</i>	<i>4</i>
4.	<i>What Are an Investigator's Responsibilities for Oversight of Other Parties Involved in the Conduct of a Clinical Trial?.....</i>	<i>5</i>
B.	PROTECTING THE RIGHTS, SAFETY, AND WELFARE OF STUDY SUBJECTS	7
1.	<i>Reasonable Medical Care Necessitated by Participation in a Clinical Trial.....</i>	<i>7</i>
2.	<i>Reasonable Access to Medical Care.....</i>	<i>7</i>
3.	<i>Protocol Violations that Present Unreasonable Risks.....</i>	<i>8</i>
	ATTACHMENT A: COPY OF FORM 1572	9
	ATTACHMENT B: INVESTIGATOR RESPONSIBILITIES	12

Guidance for Industry¹

Investigator Responsibilities—Protecting the Rights, Safety, and Welfare of Study Subjects

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This guidance provides an overview of the responsibilities of a person who conducts a clinical investigation of a drug, biological product, or medical device (an *investigator* as defined in 21 CFR 312.3(b) and 21 CFR 812.3(i)). The goal of this guidance is to help investigators better meet their responsibilities with respect to protecting human subjects and ensuring the integrity of the data from clinical investigations. This guidance is intended to clarify for investigators and sponsors FDA's expectations concerning the investigator's responsibility (1) to supervise a clinical study in which some study tasks are delegated to employees or colleagues of the investigator or other third parties and (2) to protect the rights, safety, and welfare of study subjects.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. OVERVIEW OF INVESTIGATOR RESPONSIBILITIES

In conducting clinical investigations of drugs, including biological products, under 21 CFR part 312 and of medical devices under 21 CFR part 812, the investigator is responsible for:

- Ensuring that a clinical investigation is conducted according to the signed investigator statement for clinical investigations of drugs, including biological products, or agreement for clinical investigations of medical devices, the investigational plan, and applicable regulations
- Protecting the rights, safety, and welfare of subjects under the investigator's care
- Controlling drugs, biological products, and devices under investigation (21 CFR 312.60, 21 CFR 812.100)

¹ This guidance has been prepared by the Investigator Responsibilities Working Group, which includes representatives from the Office of the Commissioner, the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and the Center for Devices and Radiological Health (CDRH) at the Food and Drug Administration.

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Although specific investigator responsibilities in drug and biologics clinical trials are not identical to the investigator responsibilities in medical device clinical trials, the general responsibilities are essentially the same. This guidance discusses the general investigator responsibilities that are applicable to clinical trials of drugs, biologics, and medical devices.

An investigator's responsibilities in conducting clinical investigations of **drugs** or **biologics** are provided in 21 CFR Part 312. Many of these responsibilities are included in the required investigator's signed statement, Form FDA-1572 (see Attachment A) (hereinafter referred to as 1572). Note that although the 1572 specifically incorporates most of the requirements directed at investigators in part 312, not all requirements are listed in the 1572. Investigators and sponsors should refer to 21 CFR Parts 11, 50, 54, 56, and 312 for a more comprehensive listing of FDA's requirements for the conduct of drug and biologics studies.²

An investigator's responsibilities in conducting clinical investigations of a **medical device** are provided in 21 CFR Part 812, including the requirement that there be a signed agreement between the investigator and sponsor (see 21 CFR 812.43(c)(4) and 812.100). The medical device regulations do not require use of a specific form for an investigator's statement; and there are additional requirements not listed above (see Attachment B). Investigators and sponsors should refer to 21 CFR Parts 11, 50, 54, 56, and 812 for a more comprehensive listing of FDA's requirements for the conduct of device studies.

Nothing in this guidance is intended to conflict with recommendations for investigators contained in the International Conference on Harmonisation (ICH) guidance for industry, *E6 Good Clinical Practice: Consolidated Guidance* (Good Clinical Practice Guidance).³

III. CLARIFICATION OF CERTAIN INVESTIGATOR RESPONSIBILITIES

This section of the guidance clarifies the investigator's responsibility to supervise the conduct of the clinical investigation and to protect the rights, safety, and welfare of participants in drug and medical device clinical trials.

A. Supervision of the Conduct of a Clinical Investigation

As stated above, investigators who conduct clinical investigations of drugs, including biological products, under 21 CFR Part 312, commit themselves to personally conduct or supervise the investigation. Investigators who conduct clinical investigations of medical devices, under 21 CFR Part 812, commit themselves to supervise all testing of the device involving human subjects. It is common practice for investigators to delegate certain study-related tasks to employees, colleagues, or other third parties (individuals or entities not under the direct supervision of the investigator). When tasks are delegated by an investigator, the investigator is responsible for providing adequate supervision of those to whom tasks are delegated. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.

² As a reminder, some investigators may be responsible for submitting certain clinical trial information to the National Institutes of Health clinical trials data bank under 42 U.S.C 282(j), 402(j) of the Public Health Service Act. Although not all investigators will be expected to meet this requirement, go to www.clinicaltrials.gov for further information about potential responsibilities.

³ Guidances, including ICH guidances, are available on the Agency's Web page. See the Web addresses on the second title page of this guidance.

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In assessing the adequacy of supervision by an investigator, FDA focuses on four major areas: (1) whether individuals who were delegated tasks were qualified to perform such tasks, (2) whether study staff received adequate training on how to conduct the delegated tasks and were provided with an adequate understanding of the study, (3) whether there was adequate supervision and involvement in the ongoing conduct of the study, and (4) whether there was adequate supervision or oversight of any third parties involved in the conduct of a study to the extent such supervision or oversight was reasonably possible.

1. What Is Appropriate Delegation of Study-Related Tasks?

The investigator should ensure that any individual to whom a task is delegated is qualified by education, training, and experience (and state licensure where relevant) to perform the delegated task. Appropriate delegation is primarily an issue for tasks considered to be clinical or medical in nature, such as evaluating study subjects to assess clinical response to an investigational therapy (e.g., global assessment scales, vital signs) or providing medical care to subjects during the course of the study. Most clinical/medical tasks require formal medical training and may also have licensing or certification requirements. Licensing requirements may vary by jurisdiction (e.g., states, countries). Investigators should take such qualifications/licensing requirements into account when considering delegation of specific tasks. In all cases, a qualified physician (or dentist) should be responsible for all trial-related medical (or dental) decisions and care.⁴

During inspections of investigation sites, FDA has identified instances in which study tasks have been delegated to individuals lacking appropriate qualifications. Examples of tasks that have been inappropriately delegated include:

- Screening evaluations, including obtaining medical histories and assessment of inclusion/exclusion criteria
- Physical examinations
- Evaluation of adverse events
- Assessments of primary study endpoints
- Obtaining informed consent

The investigator is responsible for conducting studies in accordance with the protocol (see 21 CFR 312.60, Form FDA-1572, 21 CFR 812.43 and 812.100). In some cases a protocol may specify the qualifications of the individuals who are to perform certain protocol-required tasks (e.g., physician, registered nurse), in which case the protocol must be followed even if state law permits individuals with different qualifications to perform the task (see 21 CFR 312.23(a)(6) and 312.40(a)(1)). For example, if the state in which the study site is located permits a nurse practitioner or physician's assistant to perform physical examinations under the supervision of a physician, but the protocol specifies that physical examinations must be done by a physician, a physician must perform such exams.

The investigator should maintain a list of the appropriately qualified persons to whom significant trial-related duties have been delegated.⁵ This list should also describe the delegated tasks, identify the training that individuals have received that qualifies them to perform delegated tasks

⁴ Guidance for industry, *E6 Good Clinical Practice: Consolidated Guidance*, section 4.3.1.

⁵ *Ibid*, section 4.1.5

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(e.g., can refer to an individual's CV on file), and identify the dates of involvement in the study. An investigator should maintain separate lists for each study conducted by the investigator.

2. What Is Adequate Training?

The investigator should ensure that there is adequate training for all staff participating in the conduct of the study, including any new staff hired after the study has begun to meet unanticipated workload or to replace staff who have left. The investigator should ensure that staff:

- Are familiar with the purpose of the study and the protocol
- Have an adequate understanding of the specific details of the protocol and attributes of the investigational product needed to perform their assigned tasks
- Are aware of regulatory requirements and acceptable standards for the conduct of clinical trials and the protection of human subjects
- Are competent to perform or have been trained to perform the tasks they are delegated
- Are informed of any pertinent changes during the conduct of the trial and receive additional training as appropriate

If the sponsor provides training for investigators in the conduct of the study, the investigator should ensure that staff receive the sponsor's training, or any information (e.g., training materials) from that training that is pertinent to the staff's role in the study.

3. What Is Adequate Supervision of the Conduct of an Ongoing Clinical Trial?

For each study site, there should be a distinct individual identified as an investigator who has supervisory responsibility for the site. Where there is a subinvestigator at a site, that individual should report directly to the investigator for the site (i.e., the investigator should have clear responsibility for evaluating the subinvestigator's performance and the authority to terminate the subinvestigator's involvement with the study) and the subinvestigator should not be delegated the primary supervisory responsibility for the site.

The investigator should have sufficient time to properly conduct and supervise the clinical trial. The level of supervision should be appropriate to the staff, the nature of the trial, and the subject population. In FDA's experience, the following factors may affect the ability of an investigator to provide adequate supervision of the conduct of an ongoing clinical trial at the investigator's site:

- Inexperienced study staff
- Demanding workload for study staff
- Complex clinical trials (e.g., many observations, large amounts of data collected)
- Large number of subjects enrolled at a site
- A subject population that is seriously ill
- Conducting multiple studies concurrently
- Conducting a study from a remote (e.g., off-site) location
- Conducting a study at multiple sites under the oversight of a single investigator, particularly where those sites are not in close proximity

The investigator should develop a plan for the supervision and oversight of the clinical trial at the site. Supervision and oversight should be provided even for individuals who are highly qualified

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and experienced. A plan might include the following elements, to the extent they apply to a particular trial:

- Routine meetings with staff to review trial progress, adverse events, and update staff on any changes to the protocol or other procedures
- Routine meetings with the sponsor's monitors
- A procedure for the timely correction and documentation of problems identified by study personnel, outside monitors or auditors, or other parties involved in the conduct of a study
- A procedure for documenting or reviewing the performance of delegated tasks in a satisfactory and timely manner (e.g., observation of the performance of selected assessments or independent verification by repeating selected assessments)
- A procedure for ensuring that the consent process is being conducted in accordance with 21 CFR Part 50 and that study subjects understand the nature of their participation and the risks
- A procedure for ensuring that source data are accurate, contemporaneous, and original
- A procedure for ensuring that information in source documents is accurately captured on the case report forms (CRFs)
- A procedure for dealing with data queries and discrepancies identified by the study monitor
- Procedures for ensuring study staff comply with the protocol and adverse event assessment and reporting requirements
- A procedure for addressing medical and ethical issues that arise during the course of the study in a timely manner

4. What Are an Investigator's Responsibilities for Oversight of Other Parties Involved in the Conduct of a Clinical Trial?

a. Study Staff Not in the Direct Employ of the Investigator

Staff involved directly in the conduct of a clinical investigation may include individuals who are not in the direct employ of the investigator. For example, a site management organization (SMO) may hire an investigator to conduct a study and provide the investigator with a study coordinator or nursing staff employed by the SMO. In this situation, the investigator should take steps to ensure that the staff not under his/her direct employ are qualified to perform delegated tasks (see section III.A.1) and have received adequate training on carrying out the delegated tasks and on the nature of the study (see section III.A.2), or the investigator should provide such training. The investigator should be particularly cautious where documentation needed to comply with the investigator's regulatory responsibilities is developed and maintained by SMO staff (e.g., source documents, CRFs, drug storage and accountability records, institutional review board correspondence). A sponsor who retains an SMO shares responsibility for the quality of the work performed by the SMO.

The investigator is responsible for supervising the study tasks performed by this staff, even though they are not in his/her direct employ during the conduct of the study (see section III.A.3). This responsibility exists regardless of the qualifications and experience of staff members. In the event that the staff's performance of study-related tasks is not adequate

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and cannot be made satisfactory by the investigator, the investigator should document the observed deficiencies in writing to the staff member's supervisor(s) and inform the sponsor. Depending on the severity of the deficiencies, the clinical trial may need to be voluntarily suspended until personnel can be replaced.

b. Parties Other than Study Staff

There are often critical aspects of a study performed by parties not involved directly in patient care or contact and not under the direct control of the clinical investigator. For example, clinical chemistry testing, radiologic assessments, and electrocardiograms are commonly done by a central independent facility retained by the sponsor. Under these arrangements, the central facility usually provides the test results directly to the sponsor and to the investigator. Because the activities of these parties are critical to the outcome of the study and because the sponsor retains the services of the facility, the sponsor is responsible for ensuring that these parties are competent to fulfill and are fulfilling their responsibilities to the study.

Less frequently, a study may require that investigators arrange to obtain information critical to the study that cannot be obtained at the investigator's site. For example, if the study protocol requires testing with special equipment or expertise not available at the investigator's site, the investigator might make arrangements for an outside facility to perform the test. In this case, the results are usually provided directly to the investigator, who then submits the information to the sponsor. If the investigator retains the services of a facility to perform study assessments, the investigator should take steps to ensure that the facility is adequate (e.g., has the required certification or licenses). The investigator may also institute procedures to ensure the integrity of data and records obtained from the facility providing the information (e.g., a process to ensure that records identified as coming from the facility are authentic and accurate). Procedures are particularly important when assessments are crucial to the evaluation of the efficacy or safety of an intervention or to the decision to include or exclude subjects who would be exposed to unreasonable risk.

Investigators should carefully review the reports from these external sources for results that are inconsistent with clinical presentation. To the extent feasible, and considering the specifics of study design, investigators should evaluate whether results appear reasonable, individually, and in aggregate, and they should document the evaluation. If investigators detect possible errors or suspect that results from a central laboratory or testing facility might be questionable, the investigator should contact the sponsor immediately.

c. Special Considerations for Medical Device Studies

Field clinical engineers (device sponsor employees) have traditionally played a role in some investigational device procedures (e.g., cardiology, orthopedics, and ophthalmology) by providing technical assistance to the device investigator. The field clinical engineer should be supervised by the investigator because the field clinical engineer's presence or activities may have the potential to bias the outcome of studies, may affect the quality of research data, and/or may compromise the rights and welfare of human subjects. The field clinical engineer's activities should be described in the protocol. If the field engineer has

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face-to-face contact with subjects or if the activities of the field engineer directly affect the subject, those activities should also be described in the informed consent.

B. Protecting the Rights, Safety, and Welfare of Study Subjects

Investigators are responsible for protecting the rights, safety, and welfare of subjects under their care during a clinical trial (21 CFR 312.60 and 812.100). This responsibility should include:

- Providing reasonable medical care for study subjects for medical problems arising during participation in the trial that are, or could be, related to the study intervention
- Providing reasonable access to needed medical care, either by the investigator or by another identified, qualified individual (e.g., when the investigator is unavailable, when specialized care is needed)
- Adhering to the protocol so that study subjects are not exposed to unreasonable risks

The investigator should inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and the subject agrees to the primary physician being informed.

1. Reasonable Medical Care Necessitated by Participation in a Clinical Trial

During a subject's participation in a trial, the investigator (or designated subinvestigator) should ensure that reasonable medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the trial participation. If the investigator does not possess the expertise necessary to provide the type of medical care needed by a subject, the investigator should make sure that the subject is able to obtain the necessary care from a qualified practitioner. For example, if the study involves placement of a carotid stent by an interventional neuroradiologist and the subject suffers a cerebral stroke, the neuroradiologist should assess the clinical status of the subject and arrange for further care of the subject by a neurologist. Subjects should receive appropriate medical evaluation and treatment until resolution of any emergent condition related to the study intervention that develops during or after the course of their participation in a study, even if the follow-up period extends beyond the end of the study at the investigative site.

The investigator should also inform a subject when medical care is needed for conditions or illnesses unrelated to the study intervention or the disease or condition under study when such condition or illness is readily apparent or identified through the screening procedures and eligibility criteria for the study. For example, if the investigator determines that the subject has had an exacerbation of an existing condition unrelated to the investigational product or the disease or condition under study, the investigator should inform the subject. The subject should also be advised to seek appropriate care from the physician who was treating the illness prior to the study, if there is one, or assist the subject in obtaining needed medical care.

2. Reasonable Access to Medical Care

Investigators should be available to subjects during the conduct of the trial for medical care related to participation in the study. Availability is particularly important when subjects are receiving a drug that has significant toxicity or abuse potential. For example, if a study drug has potentially fatal toxicity, the investigator should be readily available by phone or other electronic communication 24 hours a day and in reasonably close proximity to study subjects (e.g., not in

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another state or on prolonged travel). Study subjects should be clearly educated on the possible need for such contact and on precisely how to obtain it, generally by providing pertinent phone numbers, e-mail addresses, and other contact information, in writing. Prior to undertaking the conduct of a study, prospective investigators should consider whether they can be available to the extent needed given the nature of the trial.

During any period of unavailability, the investigator should delegate responsibility for medical care of study subjects to a specific qualified physician who will be readily available to subjects during that time (in the manner a physician would delegate responsibility for care in clinical practice). If the investigator is a non-physician, the investigator should make adequate provision for any necessary medical care that the investigator is not qualified to provide.

3. Protocol Violations that Present Unreasonable Risks

There are occasions when a failure to comply with the protocol may be considered a failure to protect the rights, safety, and welfare of subjects because the non-compliance exposes subjects to unreasonable risks. For example, failure to adhere to inclusion/exclusion criteria that are specifically intended to exclude subjects for whom the study drug or device poses unreasonable risks (e.g., enrolling a subject with decreased renal function in a trial in which decreased function is exclusionary because the drug may be nephrotoxic) may be considered failure to protect the rights, safety, and welfare of the enrolled subject. Similarly, failure to perform safety assessments intended to detect drug toxicity within protocol-specified time frames (e.g., CBC for an oncology therapy that causes neutropenia) may be considered failure to protect the rights, safety, and welfare of the enrolled subject. Investigators should seek to minimize such risks by adhering closely to the study protocol.

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ATTACHMENT A: COPY OF FORM 1572

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION STATEMENT OF INVESTIGATOR (TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312) (See instructions on reverse side.)	Form Approved: OMB No. 0910-0014. Expiration Date: May 31, 2009. See OMB Statement on Reverse. NOTE: No investigator may participate in an investigation until he/she provides the sponsor with a completed, signed Statement of Investigator, Form FDA 1572 (21 CFR 312.53(c)).
1. NAME AND ADDRESS OF INVESTIGATOR	
2. EDUCATION, TRAINING, AND EXPERIENCE THAT QUALIFIES THE INVESTIGATOR AS AN EXPERT IN THE CLINICAL INVESTIGATION OF THE DRUG FOR THE USE UNDER INVESTIGATION. ONE OF THE FOLLOWING IS ATTACHED. ☐ CURRICULUM VITAE ☐ OTHER STATEMENT OF QUALIFICATIONS	
3. NAME AND ADDRESS OF ANY MEDICAL SCHOOL, HOSPITAL OR OTHER RESEARCH FACILITY WHERE THE CLINICAL INVESTIGATION(S) WILL BE CONDUCTED	
4. NAME AND ADDRESS OF ANY CLINICAL LABORATORY FACILITIES TO BE USED IN THE STUDY.	
5. NAME AND ADDRESS OF THE INSTITUTIONAL REVIEW BOARD (IRB) THAT IS RESPONSIBLE FOR REVIEW AND APPROVAL OF THE	
6. NAMES OF THE SUBINVESTIGATORS (e.g., research fellows, residents, associates) WHO WILL BE ASSISTING THE INVESTIGATOR IN THE CONDUCT OF THE INVESTIGATION(S).	
7. NAME AND CODE NUMBER, IF ANY, OF THE PROTOCOL(S) IN THE IND FOR THE STUDY(IES) TO BE CONDUCTED BY THE INVESTIGATOR.	

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8. ATTACH THE FOLLOWING CLINICAL PROTOCOL INFORMATION: ☐ FOR PHASE 1 INVESTIGATIONS, A GENERAL OUTLINE OF THE PLANNED INVESTIGATION INCLUDING THE ESTIMATED DURATION OF THE STUDY AND THE MAXIMUM NUMBER OF SUBJECTS THAT WILL BE INVOLVED. ☐ FOR PHASE 2 OR 3 INVESTIGATIONS, AN OUTLINE OF THE STUDY PROTOCOL INCLUDING AN APPROXIMATION OF THE NUMBER OF SUBJECTS TO BE TREATED WITH THE DRUG AND THE NUMBER TO BE EMPLOYED AS CONTROLS, IF ANY; THE CLINICAL USES TO BE INVESTIGATED; CHARACTERISTICS OF SUBJECTS BY AGE, SEX, AND CONDITION; THE KIND OF CLINICAL OBSERVATIONS AND LABORATORY TESTS TO BE CONDUCTED; THE ESTIMATED DURATION OF THE STUDY; AND COPIES OR A DESCRIPTION OF CASE REPORT FORMS TO BE USED.	
9. COMMITMENTS: I agree to conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, rights, or welfare of subjects. I agree to personally conduct or supervise the described investigation(s). I agree to inform any patients, or any persons used as controls, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent in 21 CFR Part 50 and institutional review board (IRB) review and approval in 21 CFR Part 56 are met. I agree to report to the sponsor adverse experiences that occur in the course of the investigation(s) in accordance with 21 CFR 312.64. I have read and understand the information in the investigator's brochure, including the potential risks and side effects of the drug. I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments. I agree to maintain adequate and accurate records in accordance with 21 CFR 312.62 and to make those records available for inspection in accordance with 21 CFR 312.68. I will ensure that an IRB that complies with the requirements of 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects. I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in 21 CFR Part 312.	
INSTRUCTIONS FOR COMPLETING FORM FDA 1572 STATEMENT OF INVESTIGATOR: 1. Complete all sections. Attach a separate page if additional space is needed. 2. Attach curriculum vitae or other statement of qualifications as described in Section 2. 3. Attach protocol outline as described in Section 8. 4. Sign and date below. 5. FORWARD THE COMPLETED FORM AND ATTACHMENTS TO THE SPONSOR. The sponsor will incorporate this information along with other technical data into an Investigational New Drug Application (IND). INVESTIGATORS SHOULD NOT SEND THIS FORM DIRECTLY TO THE FOOD AND DRUG ADMINISTRATION.	
10. SIGNATURE OF INVESTIGATOR	11. DATE
(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)	
Public reporting burden for this collection of information is estimated to average 100 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:	

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Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (HFM-99)
1401 Rockville Pike
Rockville, MD 20852-1448

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

Please DO NOT RETURN this application to this address.

ATTACHMENT B: INVESTIGATOR RESPONSIBILITIES
FOR SIGNIFICANT RISK DEVICE INVESTIGATIONS

This document is intended to assist investigators in identifying and complying with their responsibilities in connection with the conduct of clinical investigations involving medical devices. Although this guidance primarily addresses duties imposed upon clinical investigators by regulations of the Food and Drug Administration (FDA), investigators should be cognizant of additional responsibilities that may derive from other sources (such as the study protocol itself, the investigator agreement, any conditions of approval imposed by FDA or the governing institutional review board, as well as institutional policy and state law).

GENERAL RESPONSIBILITIES OF INVESTIGATORS (21 CFR 812.100)

1. Ensuring that the investigation is conducted according to the signed agreement, the investigational plan, and applicable FDA regulations
2. Protecting the rights, safety, and welfare of subjects under the investigator's care
3. Controlling devices under investigation
4. Ensuring that informed consent is obtained from each subject in accordance with 21 CFR Part 50 and that the study is not commenced until FDA and IRB approvals have been obtained.

SPECIFIC RESPONSIBILITIES OF INVESTIGATORS (21 CFR 812.110)

1. Awaiting IRB approval and any necessary FDA approval before requesting written informed consent or permitting subject participation
2. Conducting the investigation in accordance with:
 - a. The signed agreement with the sponsor
 - b. The investigational plan
 - c. The regulations set forth in 21 CFR Part 812 and all other applicable FDA regulations
 - d. Any conditions of approval imposed by an IRB or FDA

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3. Supervising the use of the investigational device. An investigator shall permit an investigational device to be used only with subjects under the investigator's supervision. An investigator shall not supply an investigational device to any person not authorized under 21 CFR Part 812 to receive it.
4. Disposing of the device properly. Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator shall return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.

MAINTAINING RECORDS (21 CFR 812.140)

An investigator shall maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:

1. Correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA
2. Records of receipt, use or disposition of a device that relate to:
 - a. The type and quantity of the device, dates of receipt, and batch numbers or code marks
 - b. Names of all persons who received, used, or disposed of each device
 - c. The number of units of the device returned to the sponsor, repaired, or otherwise disposed of, and the reason(s) therefore
3. Records of each subject's case history and exposure to the device, including:
 - a. Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent
 - b. All relevant observations, including records concerning adverse device effects (whether anticipated or not), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests;
 - c. A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.
4. The protocol, with documents showing the dates of and reasons for each deviation from the protocol
5. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation

INSPECTIONS (21 CFR 812.145)

Investigators are required to permit FDA to inspect and copy any records pertaining to the investigation including, in certain situations, those which identify subjects.

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SUBMITTING REPORTS (21 CFR 812.150)

An investigator shall prepare and submit the following complete, accurate, and timely reports:

1. To the sponsor and the IRB:
 - *Any unanticipated adverse device effect* occurring during an investigation. (Due no later than 10 working days after the investigator first learns of the effect.)
 - *Progress reports* on the investigation. (These reports must be provided at regular intervals, but in no event less often than yearly. If there is a study monitor, a copy of the report should also be sent to the monitor.)
 - *Any deviation from the investigational plan* made to protect the life or physical well-being of a subject in an emergency. (Report is due as soon as possible but no later than 5 working days after the emergency occurs. Except in emergency situations, a protocol deviation requires prior sponsor approval; and if the deviation may affect the scientific soundness of the plan or the rights, safety, or welfare of subjects, prior FDA and IRB approval are required.)
 - *Any use of the device without obtaining informed consent.* (Due within 5 working days after such use.)
 - *A final report.* (Due within 3 months following termination or completion of the investigation or the investigator's part of the investigation. For additional guidance, see the discussion under the section entitled "Annual Progress Reports and Final Reports.")
 - *Any further information* requested by FDA or the IRB about any aspect of the investigation.
2. To the Sponsor:
 - *Withdrawal of IRB approval* of the investigator's part of an investigation. (Due within 5 working days of such action).

INVESTIGATIONAL DEVICE DISTRIBUTION AND TRACKING

The IDE regulations prohibit an investigator from providing an investigational device to any person not authorized to receive it (21 CFR 812.110(c)). The best strategy for reducing the risk that an investigational device could be improperly dispensed (whether purposely or inadvertently) is for the sponsor and the investigators to closely monitor the shipping, use, and final disposal of devices. Upon completion or termination of a clinical investigation (or the investigator's part of an investigation), or at the sponsor's request, an investigator is required to return to the sponsor any remaining supply of the device or otherwise to dispose of the device as the sponsor directs (21 CFR 812.110(e)). Investigators must also maintain complete, current, and accurate records of the receipt, use, or disposition of investigational devices (21 CFR 812.140(a)(2)). Specific recordkeeping requirements are set forth at 21 CFR 812.140(a).

PROHIBITION OF PROMOTION AND OTHER PRACTICES (21 CFR 812.7)

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The IDE regulations prohibit the promotion and commercialization of a device that has not been first cleared or approved for marketing by FDA. This prohibition is applicable to sponsors and investigators (or any person acting on behalf of a sponsor or investigator) and encompasses the following activities:

1. Promotion or test marketing of the investigational device
2. Charging subjects or investigators for the device a price larger than is necessary to recover the costs of manufacture, research, development, and handling
3. Prolonging an investigation beyond the point needed to collect data required to determine whether the device is safe and effective
4. Representing that the device is safe or effective for the purposes for which it is being investigated

**REQUIREMENTS FOR THE PROTECTION
OF HUMAN SUBJECTS IN RESEARCH**

- 1. REASON FOR ISSUE:** This Veterans Health Administration (VHA) Handbook establishes procedures for the protection of human subjects in Department of Veterans Affairs (VA) research and the operation of the Institutional Review Board (IRB) for VA facilities.
- 2. SUMMARY OF MAJOR CHANGES:** This Handbook was revised extensively to harmonize with the Common Rule as followed by other federal agencies. VA-specific requirements are added as appropriate. The requirements in this Handbook must be implemented no later than March 12, 2015.
- 3. RELATED ISSUES:** VHA Directive 1200, VHA Handbook 1200.01, VHA Handbook 1200.2, VHA Handbook 1200.12, VHA Handbook 1058.01, and VHA Handbook 1058.03.
- 4. RESPONSIBLE OFFICE:** The Office of Research and Development (ORD) (10P9) is responsible for the contents of this Handbook. Questions may be referred to 202-443-5600, or emailed to VHACOORDRegulatory@va.gov.
- 5. RESCISSIONS:** VHA Handbook 1200.05, dated May 2, 2012, and VHA Directive 2008-072, dated Oct. 30, 2013, are rescinded.
- 6. RECERTIFICATION:** This VHA Handbook is scheduled for recertification on or before the last working day of November, 2019.

Carolyn M. Clancy, MD
Interim Under Secretary for Health

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CONTENTS

REQUIREMENTS FOR THE PROTECTION
OF HUMAN SUBJECTS IN RESEARCH

PARAGRAPH	PAGE
1. Purpose	1
2. Background	1
3. Scope	1
4. Definitions	2
5. Assuring Compliance with this Policy	6
6. IRB Membership	8
7. IRB Functions and Operations	10
8. IRB Review of Research	12
9. Expedited Review	12
10. Criteria for IRB Approval	13
11. Review by Institution	14
12. Suspension or Termination of IRB Approval	14
13. Collaborative Research	14
14. IRB Records	16
15. General Requirements for Informed Consent	17
16. Documentation of Informed Consent	19
17. Research Involving Pregnant Women, Human Fetuses, and Neonates as Subjects	21
18. Research Involving Prisoners as Subjects	21
19. Research Involving Children as Research Subjects	22
20. Subjects Lacking Decision-Making Capacity	22

PARAGRAPH	PAGE
21. Certificates of Confidentiality	24
22. Privacy Officer and Information Security Officer Duties	25
23. HIPAA Authorization	26
24. Participation of Non-Veterans as Research Subjects	28
25. Treatment of Research-Related Injuries	29
26. International Research	29
27. Accreditation of Human Research Protection Programs	30
28. Student and Other Trainee Research	30
29. VA Investigator Responsibilities	31
30. References	34
APPENDICES	
A Categories of Exempt Research	A-1
B Activities Appropriate for Expedited Review	B-1

REQUIREMENTS FOR THE PROTECTION OF HUMAN SUBJECTS IN RESEARCH

1. PURPOSE: This Veterans Health Administration (VHA) Handbook defines the procedures for implementing the federal policy, known as the “Common Rule” and other applicable federal requirements for the protection of human subjects and must be implemented no later than March 12, 2015. **NOTE:** *All sections of rescinded VHA Handbook 1200.05, dated May 2, 2012, must be followed until the VA facility implements the requirements of this new Handbook, but no later than March 12, 2015.* **AUTHORITY:** 38 U.S.C. 501, 7331, 7334; 38 CFR 16.116, 17.32, 17.33.

2. BACKGROUND:

a. The Department of Veterans Affairs (VA) is guided by the ethical principles of respect for persons, beneficence, and justice as set forth in The Belmont Report, Ethical Principles and Guidelines for the Protection of Human Subjects of Research, regardless of who conducts the research or the source of its support. **NOTE:** *The Belmont Report may be found at <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html>.*

b. VA is one of the 18 federal departments and agencies that have agreed to follow the Common Rule for the Protection of Human Subjects, effective June 18, 1991. The Common Rule is encoded in Title 38 of the Code of Federal Regulations (CFR) Part 16. This Handbook incorporates Common Rule requirements where applicable.

3. SCOPE:

a. Except as provided in paragraph 3.(d), this policy applies to all VA research (see paragraph 4.ii.) involving human subjects (see paragraph 4.i.).

b. Investigators receiving support from other federal departments or agencies (e.g., the National Institutes of Health (NIH), Department of Defense (DoD)), or from non-Federal sources (e.g., the American Heart Association) must meet the requirements of the funding source, in addition to those of VA and other applicable federal entities. **NOTE:** *When following the requirements of the funding source would cause non-compliance with federal or VA requirements, the federal and VA requirements must be followed.*

c. When FDA-regulated products or test articles are used, FDA regulations apply regardless of funding source.

d. Research activities in which the only involvement of human subjects will be in one or more of the Common Rule categories, outlined in Appendix A, may be exempt from the provisions of this Handbook. **NOTE:** *The Common Rule exemptions may not be applied to Food and Drug Administration (FDA)-regulated research (see 21 CFR 56.104 for exemptions applied to FDA-regulated research). The Research and Development (R&D) Committee has oversight for all exempt research (see Handbook 1200.01, Research and Development Committee).*

e. VHA does not conduct planned emergency research (see 21 CFR 50.24) or classified research involving human subjects.

4. DEFINITIONS: The following definitions are intended for use within this Handbook and where appropriate reflect the Common Rule at 38 CFR 16.102 and Department of Health and Human Services (HHS) regulations at 45 CFR 46 Subparts A through D.

a. **Accreditation.** Accreditation is a comprehensive review of the Human Research Protection Program (HRPP) at a VA facility by an independent organization to ensure the program is comprehensive and maintains high ethical and professional standards. VHA selects an accrediting organization to review all VA Human Research Protection Programs.

b. **Adverse Event.** An adverse event (AE) in human subjects research is any untoward physical or psychological occurrence in a human subject participating in research. **NOTE:** *AEs are further discussed in VHA Handbooks 1058.01, Research Compliance Reporting Requirements, and 1004.08, Disclosure of Adverse Events to Patients.*

c. **Assurance.** An assurance is a written commitment to protect human research subjects and comply with the requirements of the Common Rule. **NOTE:** *Assurances are further discussed in VHA Handbook 1058.03, Assurance for Protection for Human Subjects in Research.*

d. **Certificate of Confidentiality.** A certificate of confidentiality is a document issued by a component of HHS pursuant to The Public Health Service Act Section 301(d), Title 42 United States Code (U.S.C.) 241(d), to protect the privacy of individuals who are subjects of certain specified research activities by authorizing investigators to withhold from all persons not connected with the conduct of such research the names or other identifying characteristics of such subjects. Persons so authorized to protect the privacy of such individuals may not be compelled in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals.

e. **Children.** Children are persons who have not attained the legal age to consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted.

f. **Clinical Investigation.** The FDA considers the term “clinical investigation” to mean any experiment that involves a test article and one or more human subjects, and that either:

(1) Meets the requirements for prior submission to the FDA under Sections 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, as codified at 21 U.S.C. 355(i) and 360j(g) respectively; or

(2) Does not meet the requirements for prior submission to the FDA under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit (21 CFR 56.102(c)).

g. **Collaborative Research.** Collaborative research involves investigators from more than one institution. Collaborative research may include VA and non-VA institutions but does not

include research conducted under a Cooperative Research and Development Agreement (CRADA) with a pharmaceutical company or other non-Federal partners.

h. **Continuing Noncompliance.** Continuing noncompliance is a persistent failure to adhere to the laws, regulations, or policies governing human subjects research. **NOTE:** *Continuing noncompliance is further discussed in VHA Handbook 1058.01.*

i. **De-identified Information.** De-identified information is health information that is presumed not to identify an individual and with respect to which there is no reasonable basis to believe that the information can be used to identify an individual because the 18 Patient Identifiers described in the HIPAA Privacy Rule have been removed.

j. **Fetus.** A fetus is the product of conception from the time of implantation until delivery.

k. **Human Research Protection Program.** The HRPP is a comprehensive system to ensure the protection of human subjects participating in research. The HRPP consists of a variety of individuals and committees such as: the VA facility Director, Associate Chief of Staff (ACOS) for Research and Development (R&D), the Administrative Officer (AO) for R&D, the R&D Committee, the Institutional Review Board (IRB), other committees or subcommittees addressing human subjects protection (e.g., Biosafety, Radiation Safety, Radioactive Drug Research, Conflict of Interest), investigators, IRB staff, research staff, health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer), compliance officers, information security officers, privacy officers, and research pharmacy staff. The objective of this system is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

l. **Human Subject.** A human subject is a living individual about whom an investigator (whether professional or student) conducting research obtains: (1) data through intervention or interaction with the individual or (2) identifiable private information. Individuals who receive test articles or who serve as controls in clinical investigations, including clinical investigations as defined under FDA regulations in 21 CFR 50.3, 312.3(b), and 812.3(h), are also considered human subjects for the purposes of this Handbook.

m. **In Vitro Fertilization.** In vitro fertilization is any fertilization of human ova that occurs outside the body of a female, either through a mixture of donor human sperm and ova or by any other means.

n. **Institutional Official.** The Institutional Official (IO) is the individual legally authorized as signatory official to commit an institution to an assurance. The IO is responsible for ensuring that the institution's HRPP functions effectively and that the institution provides the resources and support necessary to comply with all requirements applicable to research involving human subjects. The Principal Deputy Under Secretary for Health is the IO for VHA Central Office, and VA facility Directors are the IOs for local VA facilities. The IO serves as the official representative of the institution to external agencies and oversight bodies, and provides all written communication with external departments, agencies, and oversight bodies.

o. **Institutional Review Board.** An IRB is a board, committee, or other group formally designated by an institution to review, approve, require modification, disapprove, and conduct

continuing oversight of human subject research in accordance with the Common Rule (38 CFR Part 16) and other applicable regulations. **NOTE:** *For the purposes of this Handbook, unless otherwise specified, references to IRB include any IRB which is responsible for approval and monitoring of a particular research project.*

p. **Interaction.** Interaction includes communication or interpersonal contact between investigator and subject.

q. **Intervention.** Intervention includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

r. **Investigator.** An investigator is an individual who conducts research, including the principal investigator, co-investigators, sub-investigators, and local site investigators (*see paragraph 29*). **NOTE:** *The responsibilities of VA investigators are further discussed in VHA Handbook 1200.01.*

s. **Legally Authorized Representative.** A legally authorized representative (LAR) is an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. **NOTE:** *An individual who is qualified as a LAR to provide informed consent on behalf of a prospective research subject may not always qualify as a personal representative for purposes of consent to use or disclose a subject's protected health information (PHI) (i.e., signing a Health Insurance Portability and Accountability Act (HIPAA) authorization). Therefore, in circumstances involving authorization for use or disclosure of a human subject's PHI, the investigator must ensure the LAR meets the requirements of a personal representative under HIPAA and the Privacy Act of 1974 (legal guardian or power of attorney) prior to the LAR's signing a HIPAA authorization (see VHA Handbook 1605.1, Privacy and Release of Information).*

t. **Minimal Risk.** Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

u. **Multi-site Research.** Multi-site research involves more than one research site. Multi-site research may include VA and non-VA institutions, and may include both collaborative research and research conducted under a CRADA with a pharmaceutical company or other non-Federal entity. **NOTE:** *See the definition for Collaborative Research at paragraph 4.g.*

v. **Neonate.** Neonate means a newborn within the first 4 weeks of birth.

w. **Nonprofit Research and Education Corporations.** VA-affiliated nonprofit research and education corporations (NPC) are authorized by Congress under 38 U.S.C. 7361-7366 to provide flexible funding mechanisms for the conduct of research and education at one or more VA facilities. Research approved by a facility R&D Committee and education approved by the facility Education Committee is considered to be a VA research project or a VA education activity respectively, regardless of the source of funding, the entity administering the funds, or

the research or education site (see [VHA Handbook 1200.17, Department of Veterans Affairs Nonprofit Research and Education Corporations](#) authorized by 38 U.S.C. Sections 7361-7366).

x. **Principal Investigator.** A principal investigator (PI) is a qualified individual who directs a research project or research program. The PI oversees scientific, technical, and day-to-day management of the research. In the event of research conducted by a team of individuals, the PI is the responsible leader of the research team.

y. **Pregnancy.** Pregnancy encompasses the period of time from implantation until delivery.

z. **Private Information.** Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a health record). Private information must be individually identifiable (i.e., the identity of the subject is provided or may readily be ascertained or associated with the information) in order for obtaining the information to constitute research involving human subjects (38 CFR 16.102(f)).

aa. **Research.** Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. Clinical investigations, including clinical investigations as defined under FDA regulations in 21 CFR 50.3, 312.3(b), and 812.3(h), are considered research for purposes of this Handbook. **NOTE:** *Research activities are further discussed in VHA Handbook 1058.05.*

bb. **Research Records.** Research records include, but are not limited to, IRB and R&D Committee records, records of all observations, subject recruitment activities, other data relevant to the investigation, progress notes, research study forms, surveys, questionnaires, and other documentation regarding the study (see VHA Handbook 1907.01, Health Information and Health Records).

cc. **Research and Development Committee.** The R&D Committee is a committee responsible, through the Chief of Staff (COS) to the VA facility Director, for oversight of the facility's research program and for maintenance of high standards throughout that program (see VHA Handbook 1200.01).

dd. **Research Protocol.** A research protocol details the aims and objectives of a research study, scientific rationale, the methods used to carry out the research, and how data will be analyzed. For human subjects research it also entails how subjects will be accessed/recruited, any foreseeable risks, and how these risks will be mitigated. **NOTE:** *The protocol for social or behavioral research is sometimes referred to as the "Research Plan" or "Research Purpose and Methodology."*

ee. **Serious Adverse Event.** A serious adverse event (SAE) is an AE in human subjects research that results in death, a life-threatening experience, inpatient hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, congenital

anomaly, or birth defect. An AE is also considered serious when medical, surgical, behavioral, social, or other intervention is needed to prevent such an outcome. **NOTE:** SAE's are also discussed at 21 CFR 312.32(a) and in VHA Handbook 1058.01; disclosure of adverse events to patients is discussed in VHA Handbook 1004.08.

ff. **Serious Noncompliance.** Serious noncompliance is a failure to adhere to the laws, regulations, or policies governing human subjects research that may reasonably be regarded as:

(1) Involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others; or

(2) Substantively compromising the effectiveness of a facility's human subjects research protection or human subjects research oversight programs. **NOTE:** Serious noncompliance is further discussed in VHA Handbook 1058.01.

gg. **Unanticipated or Unexpected.** The terms unanticipated and unexpected refer to an event or problem in VA research that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol-related documents and the characteristics of the study population.

hh. **VA Investigator.** A VA investigator is any individual who conducts research approved by the VA R&D committee while acting under a VA appointment on VA time, including full and part-time compensated employees, trainees, without compensation (WOC) employees, and individuals appointed or detailed to VA under the Intergovernmental Personnel Act (IPA) of 1970. **NOTE:** Contractors cannot be VA Investigators.

ii. **VA Research.** VA research is research that is conducted by VA investigators (serving on compensated, WOC, or IPA appointments) while on VA time. The research may be funded by VA, by other sponsors, or be unfunded. VA research must have R&D Committee approval. **NOTE:** VA research is discussed in VHA Handbook 1200.01 and VHA Handbook 1200.2, Research Business Operations.

5. ASSURING COMPLIANCE WITH THIS POLICY:

a. Each VA facility engaged in research covered by this Handbook must obtain a Federal-wide Assurance (FWA) prior to conducting any human subjects research. The IO is the individual legally authorized as signatory official to commit an institution to a FWA. **NOTE:** VA facilities filing an FWA and VA Addendum must submit applications and renewals through the Office of Research Oversight (ORO) (see VHA Handbook 1058.03).

b. **Responsibilities of the Institutional Official.** The IO is responsible for overseeing the facility's research program, and this responsibility cannot be delegated. The IO is responsible for the creation and implementation of an HRPP for research involving human subjects. The exact composition of the HRPP depends on the specific facility, the resources of the facility, and the type, size, and complexity of its research program. The IO's responsibilities for the facility's HRPP include, but are not limited to:

(1) Overseeing the R&D Committee, IRB, and other applicable subcommittees of the R&D Committee, facility research office, and all VA investigators and VA research staff who conduct human subjects research at that facility.

(2) Delegating authority in writing for respective roles and responsibilities for the HRPP. This delegation of authority must provide the organizational structure and ensure leadership for oversight activities for all human subjects research conducted at or by the facility.

(3) Ensuring provision of adequate resources to support the operations of the HRPP.

(4) Ensuring independence of the IRB.

(5) Ensuring that a procedure is in place to review and approve recruiting documents, flyers, and advertisements for research that is not VA research prior to being posted or distributed in any form within or on the premises of a VA facility. Posting or distributing may include announcing, distributing, publishing, or advertising the study either electronically, by hard copy, or other means to anyone, including Veterans, clinicians, or other staff (see ORD guidance at <http://www.research.va.gov/resources/policies/default.cfm>).

c. All research subject to this Handbook must be reviewed and approved by an IRB designated in the facility's FWA (the IRB of Record), and will be subject to continuing review and oversight by the IRB of Record. **NOTE:** *Research that meets the exempt categories are not subject to IRB review but must be reviewed by the R&D Committee (see Appendix A).*

d. The IO is responsible for ensuring that any IRB designated as an IRB of Record for the facility is established in accordance with the requirements of this Handbook and registered through the ORO to the Office for Human Research Protections (OHRP).

(1) The facility's IRB(s) of Record may include the facility's own IRB(s), the VHA Central Office IRB (VA Central IRB), an IRB of another VA facility, the IRB(s) of its affiliated medical or dental school, or an IRB of another federal agency; and

(2) When the facility engages the services of another entity's IRB as its IRB of Record, the IO is responsible for:

(a) Establishing and signing a memorandum of understanding (MOU) or Authorizing Agreement with other VA facilities or external organization(s) providing IRB services (see VHA Handbook 1058.03 and MOU Checklist: <http://www.va.gov/ORO/orochecklists.asp>); and

(b) Ensuring that at least two VA-compensated (minimum 1/8th full-time employee equivalent) staff from the facility are appointed as voting members to each IRB of Record except for the VA Central IRB (see VA Central IRB Standard Operating Procedures (SOP)) or a central IRB of another federal agency (e.g., National Cancer Institute Central IRB). A small VA facility with fewer than ten active protocols is only required to appoint one voting member and one alternate voting member to ensure consistent representation. **NOTE:** *At least one VA voting member of the IRB must be in attendance when their facility's research is discussed at a convened meeting.*

(c) Obtaining approval of the Chief Research and Development Officer (CRADO) if the VA facility wants to establish a new HRPP or change their IRB of Record.

e. A VA facility's own internal IRB cannot serve as an IRB of Record for any non-VA entity except a DoD facility or a VA NPC.

f. Research funded through a VA NPC is considered VA research and the NPC must use the IRB(s) of Record and the R&D Committee of the VA facility that will conduct the research (see VHA Handbook 1200.17).

g. Neither the VA facility nor the investigator may engage the services of another IRB for the purposes of avoiding the requirements or determinations of the IRB of Record.

NOTE: All IRBs regardless of the type described above must meet all the IRB requirements described in this Handbook.

6. IRB MEMBERSHIP:

a. Each IRB must have at least five voting members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution(s) for which it reviews research. The IRB must be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB must be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable local, VA and other federal requirements, and standards of government ethics and professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or physically or mentally disabled persons, consideration must be given to the inclusion of one or more individuals on the IRB who are knowledgeable about and are experienced in working with these subjects. IRBs serving VA should also consider including a Veteran or Veteran's representative.

b. Every nondiscriminatory effort should be made to ensure that no IRB consists entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. No IRB may consist entirely of voting members of one profession.

c. Each IRB must include at least one voting member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. Physicians, dentists, nurses, pharmacists, social workers, other clinicians, statisticians, and allied health professionals are considered to be scientists.

d. Each IRB must include at least one voting member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution. Retired VA employees who are receiving VA retirement benefits are considered to

be affiliated when they are members of a VA IRB. **NOTE:** *Veterans who receive their care at the facility, but have never been employed by VA, would not be considered affiliated.*

e. No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

f. An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

g. VA facilities must maintain accurate membership rosters for their designated IRB(s) of Record and submit the roster(s) to ORO as required by VHA Handbook 1058.03. The roster must list IRB members identified by name, earned degrees, representative capacity, indications of experience such as board certifications, licenses, etc., sufficient to describe each member's primary anticipated contributions to IRB deliberations, and any employment or other relationship between each member and the institution (e.g., full-time employee, part-time employee, member of governing panel or board, paid or unpaid consultant).

h. VA facility research office staff including, but not limited to, the ACOS for R&D, the AO for R&D, and IRB administrative staff may not serve as voting members of the facility's IRB. They may serve as ex officio, non-voting members; however, they and the IRB must be sensitive to any potential, actual, apparent, or perceived conflicts of interest and appropriately manage such conflicts. **NOTE:** *Ex officio members are for purposes of this Handbook not allowed to be voting members of the IRB.*

i. Research Compliance Officers (RCOs) may act as consultants to the facility's IRB, but may not serve as voting or non-voting members of the IRB. RCOs may attend IRB meetings when requested by the IRB or as specified by the IRB's standard operating procedures (SOPs). RCO's must be aware of and manage any potential, actual, apparent, or perceived conflicts of interest that arise because of their role. **NOTE:** *RCOs are further discussed in VHA Handbook 1058.01.*

j. The Privacy Officer (PO) and the Information Security Officer (ISO) serve in an advisory capacity to the facility's IRB as either non-voting members or as consultants (see paragraph 22 for specific roles and responsibilities).

k. Facility Directors, their administrative staff, COS, other facility senior administrators such as Associate or Assistant Directors or Chief Nurse, and NPC Administrative Staff may observe IRB meetings, but may not serve as voting or non-voting members of the facility's IRB.

l. If alternate members are appointed to the facility's IRB, the IRB's written procedures must describe the appointment and function of alternate members, and the IRB membership roster must identify by name the primary member(s) for whom each alternate member may substitute. The alternate members must have qualifications similar to the member they replace.

m. The IO appoints IRB voting members in writing. Appointment procedures for ex officio, non-voting members are made according to local SOPs and any other applicable VA

requirements. Voting members of VA IRBs and VA representatives to external IRB(s) of Record are appointed for a period of up to 3 years. They may be re-appointed to new terms of up to 3 years without a break in service at the end of each term. **NOTE:** *There are not a maximum number of terms for IRB members as long as the composition of the IRB meets all requirements.*

n. The Chair, Co-Chair(s), and Vice Chair(s) of a VA-operated IRB must be paid VA employees (i.e., not holding a WOC or IPA appointment at VA). **NOTE:** *This does not apply to IRBs of record external to the VA.*

(1) There may be one IRB Chair, Co-chairs, or a Chair and Vice Chair(s). Each may serve as a voting member of the IRB pursuant to IRB SOPs.

(2) The Chair and, when applicable, Co-chair(s) or Vice Chair(s), are appointed by the IO for a term of up to 3 years, and may be re-appointed indefinitely.

7. IRB FUNCTIONS AND OPERATIONS:

a. **Standard Operating Procedures.** The IRB must establish written SOPs that include, but are not limited to procedures for:

(1) Conducting initial and continuing review of research and reporting findings and actions to the investigator and to the R&D Committee;

(2) Determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review;

(3) Ensuring prompt reporting by an investigator to the IRB of proposed changes in a research activity, and ensuring that such changes in approved research, during the period for which IRB approval has already been given, are not initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject;

(4) Ensuring prompt reporting to the IRB, appropriate institutional officials, and ORO of: (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB and (ii) any suspension or termination of IRB approval. **NOTE:** *Requirements for reporting to ORO are discussed in VHA Handbook 1058.01;*

(5) Determining whether a study meets the criteria in Appendix A for exemption from the requirements of the Common Rule. **NOTE:** *The investigator may not self-certify that a study is exempt. The R&D Committee or another subcommittee of the R&D Committee must be responsible for initial and continuing oversight of the exempt research (see VHA Handbook 1200.01);*

(6) Observing, or having a third party observe, research activities, including the informed consent process, when the IRB determines this to be appropriate;

(7) Conducting expedited review and reporting findings and actions to the IRB, R&D Committee, and investigator; and

(8) Training and education of the IRB Chair, voting members, and alternates in human subjects protections, ethics, and regulatory requirements.

NOTE: *When the IRB of Record is that of the academic affiliate, the SOPs related to the review of VA research for all affiliate IRBs reviewing VA research must be consistent with this Handbook and all regulations applicable to VA research.*

b. **IRB Functions.** Except when an expedited review procedure is used (see paragraph 9), the IRB must review proposed VA research at convened meetings at which a majority of the voting members (quorum) of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it must receive the approval of a majority of those members present at the meeting.

(1) The IRB may vote to approve, require modifications in (to secure approval), or disapprove a protocol.

(2) The IRB determines the approval period (not to exceed 1 year) and whether verification should be required from sources other than the investigators that no substantive modifications have occurred since previous IRB review.

(3) The IRB's review includes a review of the research protocol, the application to the IRB, and all other relevant documents (e.g., informed consent forms, surveys, advertising materials, HIPAA authorization, and investigator's brochure) submitted to the IRB.

(4) A quorum must be present during the review and approval of the study. If the required number and type of voting members are not present at any point during a meeting, a quorum must be restored before any discussion of, or action on, issues requiring a vote may occur.

c. **IRB Minutes.** Minutes of IRB meetings shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

(1) For protocols reviewed by the convened IRB, the IRB minutes shall document that the IRB determined that all of the criteria for approval of the research (see paragraph 10) were satisfied.

(2) If the IRB approves a consent procedure which does not include, or which alters, any of the elements of informed consent (see paragraph 15.e.), or waives the requirement to obtain a signed informed consent document (see paragraph 16.c.), it must document that all criteria for the waiver have been satisfied.

(3) IRB minutes must be submitted to the R&D Committee in accordance with local SOPs. When an affiliate IRB is the IRB of Record, the affiliate may either:

(a) Provide VA with unredacted copies of meeting minutes, or

(b) Provide VA with redacted copies of meeting minutes and permit relevant VA personnel (including, but not limited to, ORO staff, local VA Research Office staff, local RCOs, and R&D Committee members) to review the unredacted meeting minutes within two business days of a written request from VA. Such review may occur at the affiliate site during normal business hours, or as otherwise mutually acceptable to VA and the affiliate.

8. IRB REVIEW OF RESEARCH: An institution's IRB of Record shall:

a. Review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this Handbook;

b. Require that information given to subjects as part of informed consent is in accordance with paragraph 15 of this Handbook. The IRB may require that information, in addition to that specifically mentioned in paragraph 15 of this Handbook, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects;

c. Require documentation of informed consent or waive documentation in accordance with paragraph 16 of this Handbook;

d. Notify investigators and the R&D Committee in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing;

e. Conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year; and

f. Have authority to observe or have a third party observe the consent process and the research.

9. EXPEDITED REVIEW:

a. An IRB may use the expedited review process to review either or both of the following:

(1) Any of the categories of research described in Appendix B and found by the reviewer(s) to involve no more than minimal risk; and

(2) Minor changes in previously approved research during the period for which approval is authorized.

b. In the expedited review process, the IRB Chair may carry out the review or delegate the review to one or more experienced reviewers from among voting IRB members.

c. The reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth in paragraph 8.

d. The decision and the expedited review eligibility category must be included in the IRB minutes of the next available convened IRB meeting and in the written notification to the investigator and R&D Committee.

10. CRITERIA FOR IRB APPROVAL:

a. In order to approve research covered by this Handbook the IRB must determine that all of the following requirements are satisfied:

(1) Risks to human subjects are minimized in the following ways:

(a) By using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk; and

(b) Whenever appropriate, are already being performed on the subjects for diagnostic or treatment purposes. **NOTE:** *The IRB must document its determination on the level of risk either in the IRB minutes or the written communication to the investigator;*

(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, and the importance of the knowledge that may be reasonably expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits the subjects would receive even if not participating in the research). The IRB is not to consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility;

(3) Selection of subjects is equitable. In making this assessment, the IRB takes into account the purposes of the research and the setting in which the research is to be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, physically or mentally-disabled persons, and economically or educationally disadvantaged persons;

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by paragraph 15;

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by paragraph 16;

(6) When appropriate, the research protocol makes adequate provision for monitoring the data collected to ensure the safety of subjects; and

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

b. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, physically or mentally-disabled persons, or educationally or economically disadvantaged persons, or require special considerations such as pregnant women, the protocol must include additional safeguards to protect the rights and welfare of these subjects.

c. VA also requires the following criteria to be met:

(1) Privacy and confidentiality provisions must take into consideration the requirements of Standards for Privacy of Individually-Identifiable Health Information (HIPAA Privacy Rule), 45 CFR Parts 160 and 164, and other laws regarding protection and use of Veterans' and others information, including the Privacy Act of 1974, 5 U.S.C. 552a; VA Claims Confidentiality Statute, 38 U.S.C. 5701; Confidentiality of Drug Abuse, Alcoholism and Alcohol Abuse, Infection with Human Immunodeficiency Virus (HIV), and Sickle Cell Anemia Medical Records, 38 U.S.C. 7332; and Confidentiality of Healthcare Quality Assurance Review Records, 38 U.S.C. 5705 (see VHA Handbook 1605.1);

(2) Relevance of the research to the mission of VA and the Veteran population that it serves must be considered by the IRB. If non-Veterans will be included, the protocol and related materials must justify the inclusion of non-Veterans; and

(3) The IRB must ensure that mechanisms are implemented to manage, reduce, or eliminate potential, actual, or perceived conflicts of interest related to all aspects of the research, including financial interests, clinical roles (for example, investigator-patient relationships), and other professional or personal roles.

11. REVIEW BY INSTITUTION:

a. Research that has been approved by the IRB may be subject to further appropriate review and approval or disapproval by officials of the institution, but those officials may not approve human subjects research if it has not been approved by the IRB.

b. An IRB-approved research activity may be disapproved by the IO, the R&D Committee, or ORD. If a research activity is disapproved by the IRB, or modifications to the research are required by the IRB, the disapproval or need for modification cannot be overruled by any other authority (e.g., IO or R&D Committee).

c. The R&D Committee must provide the final approval before the research can be initiated in accordance with VHA Handbook 1200.01.

12. SUSPENSION OR TERMINATION OF IRB APPROVAL: The IRB has authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements, or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval must include a statement of the reasons for the IRB's action and must be reported promptly to the investigator, appropriate IO(s), ORO (in accordance with VHA Handbook 1058.01), and appropriate federal agencies according to applicable local, VA, and other federal requirements. **NOTE:** *The R&D Committee and the IO also have authority to suspend or terminate their approval of research (see Handbook 1200.01).*

13. COLLABORATIVE RESEARCH: This section addresses collaborations between VA and non-VA investigators. Collaboration is encouraged when VA investigators have a substantive role in the design, conduct, and/or analysis of the research. VA may also serve as a Coordinating Center for collaborative studies. **NOTE:** *For purposes of this Handbook, collaborative studies do not include studies conducted under a CRADA with pharmaceutical companies or other for-profit entities.*

a. **IRB of Record Approval.** Each institution is responsible for safeguarding the rights and welfare of human subjects and providing oversight of the research activities conducted at that institution.

(1) Each collaborating institution engaged in human subjects research must obtain approval from its IRB of Record and hold a FWA or another assurance acceptable to VA, e.g. DoD assurance.

(2) VA investigators must submit a protocol or other documentation to their VA IRB of Record that delineates which research activities will be conducted by VA.

(3) Each institution engaged in the collaborative research must use the informed consent document and HIPAA authorization required by their respective institutional policies for subjects recruited from that institution, or procedures requiring participation of the subject at that institution. The informed consent document may contain information on the project as a whole as long as the document clearly describes which procedures will be performed at VA and which will be performed at other institutions.

(a) The VA informed consent document must clearly state when procedures mentioned at other institutions are part of the VA's portion of the study.

(b) The informed consent document and HIPAA authorization must be consistent and include information describing the following:

1. PHI to be collected and/or used by the VA research team;
2. PHI to be disclosed to the other institutions; and
3. Purpose for which the PHI may be used.

(c) **Waivers.** PHI obtained in research for which the IRB of Record has waived the requirements to obtain a HIPAA authorization and a signed informed consent document may not be disclosed outside VA unless the VA facility Privacy Officer ensures and documents VA's authority to disclose the PHI to another institution. A waiver of HIPAA authorization is not sufficient to fulfill the requirements of other applicable privacy regulations such as the Privacy Act of 1974 (5 U.S.C. 552a).

b. **Research Data.** The protocol, addendum, and/or IRB of Record application must describe the data to be disclosed to collaborators, the entity(ies) to which the data are to be disclosed, and how the data are to be transmitted. This includes data from individual subjects as well as other data developed during the research such as the analytic data and the aggregate data.

(1) Each VA facility must retain a complete record of all data obtained during the VA portion of the research in accordance with privacy requirements, the Federal Records Act, and VHA Records Control Schedule (RCS) 10-1.

(2) All disclosures and data transmission must meet privacy and security requirements per VA Directive 6500, VA Handbook 6500, and VHA Handbook 1605.1.

c. **Written agreements.** Collaborative research involving non-VA institutions may not be undertaken without a signed written agreement (e.g., a CRADA or a Data Use Agreement (DUA)) that addresses such issues as the responsibilities of each party, the ownership of the data, and the reuse of the data for other research. **NOTE:** *Any reuse must be consistent with the protocol, the informed consent document, and the HIPAA authorization.*

14. IRB RECORDS:

a. An institution, or when appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities, including the following:

(1) Copies of all research protocols reviewed, scientific evaluations, if any, that accompany the proposals, approved consent documents, progress reports submitted by investigators, and reports of injuries to subjects;

(2) Minutes of IRB meetings as described in paragraph 7.c.;

(3) Records of continuing review activities;

(4) Copies of all correspondence between the IRB and the investigators;

(5) A roster of IRB members in the same detail as described in paragraph 6.g. IRB records must include a resume or Curriculum Vitae for each voting IRB member that is updated at the time of appointment or reappointment;

(6) Written procedures for the IRB in the same detail as described in paragraph 7.a.; and

(7) Statement of significant new findings provided to subjects, as required by paragraph 15.d.(5).

b. All records must be accessible for inspection and copying by authorized representatives of VA, ORO, OHRP, FDA, and other authorized entities at reasonable times and in a reasonable manner. Records should be disposed in accordance with VHA RCS 10-1.

c. IRB records are the property and the responsibility of the local research office. The local VA facility must designate where the records will be maintained or stored. **NOTE:** *Records of an affiliate IRB are addressed in the MOU (see paragraph 5.d.(2)(a) and VHA Handbook 1058.03). The MOU must ensure that all applicable federal and VA regulations are met.*

15. GENERAL REQUIREMENTS FOR INFORMED CONSENT:

a. **General Requirements.** Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

(1) The information that is given to the subject or the representative must be in language understandable to the subject or the representative.

(2) No informed consent process, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive, or appear to waive, any of the subject's legal rights, or releases or appears to release, the investigator, the sponsor, the institution or its agents from liability for negligence.

b. **Basic Elements of Informed Consent.** Except as provided in paragraph 15.e., in seeking informed consent the following information must be provided to each subject:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures that are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others that may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) An explanation as to whether any compensation is available, and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained (see paragraph 25);

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of research-related injury to the subject; and

(8) A statement that participation is voluntary, refusal to participate involves no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

c. **Additional Elements Required by VA.** The following additional elements of informed consent are required for VA research:

- (1) Any payments the subject is to receive for participating in the study;
- (2) Any real or apparent conflict of interest by investigators where the research will be performed; and
- (3) A statement that VA will provide treatment for research related injury in accordance with applicable federal regulations (see paragraph 25).

d. **Additional Elements of Informed Consent.** When appropriate, one or more of the following elements of information shall also be provided to each subject:

- (1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or becomes pregnant) that are currently unforeseeable;
- (2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
- (3) Any additional costs to the subject that may result from participation in the research;
- (4) The consequences of a subject's decision to withdraw from the research and procedures for orderly and safe termination of participation by the subject;
- (5) A statement that any significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject;
- (6) The approximate number of subjects to be entered in the study; and
- (7) When appropriate, a statement that informs VA research subjects that they or their insurance will not be charged for any costs related to the research. **NOTE:** *Some Veterans are required to pay copayments for medical care and services specifically related to their medical care provided by VA. These co-payment requirements will continue to apply to medical care and services that are not part of the research procedures or interventions.*

e. **Waiver or Alteration of Informed Consent.** The IRB may approve an informed consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided that:

(1) The IRB finds and documents that the research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:

(a) Public benefit or service programs (also see Appendix A, paragraph 6); procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those

programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs; and

(b) The research could not practicably be carried out without the waiver or alteration; **or**

(2) The IRB finds and documents that:

(a) The research involves no more than minimal risk to the subjects;

(b) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(c) The research could not practicably be carried out without the waiver or alteration; and

(d) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

f. The informed consent requirements in this Handbook are not intended to preempt any applicable federal, state, or local laws that require additional information to be disclosed in order for informed consent to be legally effective.

g. Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care to the extent that the physician is permitted to do so under applicable federal, state, or local law.

16. DOCUMENTATION OF INFORMED CONSENT:

a. Except as provided in paragraph 16.c., informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's LAR. A copy shall be given to the person signing the form.

b. Except as provided in paragraph 16.d., the informed consent document may be either of the following:

(1) A written consent document that embodies the elements of informed consent described in paragraph 15. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or

(2) A short form written consent document stating that the elements of informed consent required in paragraph 15 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said in the oral presentation to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form. **NOTE:** *The IRB cannot waive the requirement for a witness or witness signature when the short form consent is used.*

c. The IRB may waive the requirement for the investigator to obtain a signed consent document for some or all subjects if it finds either:

(1) That the only record linking the subject and the research is the consent document and the principal risk is potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

d. In cases in which the documentation requirement is waived, IRB may require the investigator to provide subjects with a written statement regarding the research.

e. **VA-specific Requirements.**

(1) The consent form must be the most recent IRB-approved consent form that includes all the required elements and, as appropriate, additional elements. The IRB approval must be documented on the consent form indicating the date of approval.

(2) The informed consent document must be signed and dated by:

(a) The subject or the subject's LAR; and

(b) The person obtaining the informed consent. However, the IRB may waive this requirement for the signature of the person obtaining consent (even where the signature of the subject or the LAR continues to be required) where there is no physical contact with the subject (e.g., where the only contact with the subject is by telephone or mail).

(c) Consent may be obtained electronically so long as the informed consent process meets all requirements in paragraph 16 of this Handbook and VA requirements; and:

(1) Authentication controls on electronic consent provide reasonable assurance that such consent is rendered by the proper individual; and

(2) The subject dates the consent as is typical or that the software provides the current date when signed.

f. **Photography, Video and/or Audio Recording for Research Purposes.** The informed consent for research must include information describing any photographs, video, and/or audio recordings to be taken or obtained for research purposes, how the photographs, video, and/or audio recordings will be used for the research, and whether the photographs, video, and/or audio recordings will be disclosed outside VA.

(1) An informed consent to take a photograph, video and/or audio recording cannot be waived by the IRB.

(2) The consent for research does not give legal authority to disclose the photographs, video, and/or audio recordings outside VA. A HIPAA authorization is needed to make such disclosures.

17. RESEARCH INVOLVING PREGNANT WOMEN, HUMAN FETUSES, AND NEONATES AS SUBJECTS:

a. Research that involves provision of in vitro fertilization services cannot be conducted by VA investigators while on official duty, or at VA facilities, or at VA-approved off-site facilities.

NOTE: *Prospective and retrospective studies that enroll or include pregnant subjects who conceived through in vitro fertilization or other artificial reproductive technologies are permitted.*

b. Research in which the focus is either a fetus, or human fetal tissue, in-utero or ex-utero (or uses human fetal tissue), cannot be conducted by VA investigators while on official duty, at VA facilities, or at VA-approved off-site facilities. Use of stem cells shall be governed by the policy set by NIH for recipients of NIH research funding.

c. VA investigators cannot conduct interventions in research that enroll neonates while on official duty, or at VA facilities, or at VA-approved off-site facilities. Prospective observational and retrospective record review studies that involve neonates or neonatal outcomes are permitted.

d. Women who are known to be pregnant and/or their fetuses may be involved in research if all of the requirements of 45 CFR 46.204 are met including informed consent requirements and the following ethical and scientific criteria:

(1) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

(2) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or fetus. If there is no such prospect of benefit, then the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means;

(3) Any risk is the least possible for achieving the objectives of the research; and

(4) The VA medical facility Director certifies that the medical facility has sufficient expertise in women's health to conduct the proposed research (see guidance at <http://www.research.va.gov/resources/policies/default.cfm>).

18. RESEARCH INVOLVING PRISONERS AS SUBJECTS:

a. Research involving prisoners cannot be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities unless a waiver has been granted by the CRADO. **NOTE:** *Refer to the ORD Web site at*

<http://www.research.va.gov/resources/policies/default.cfm> for details on the procedures for waiver applications.

b. If such a waiver is granted, the research must comply with the requirements of 45 CFR 46.301 - 46.306. **NOTE:** A link to these requirements is provided on the ORD Web site at: <http://www.research.va.gov/resources/policies/default.cfm>.

19. RESEARCH INVOLVING CHILDREN AS RESEARCH SUBJECTS:

a. VA is authorized to care for Veterans and to conduct research that supports the mission of VHA and that enhances the quality of health care delivery to Veterans. Therefore, research involving children must be reviewed carefully by the IRB for its relevance to VA and must not be greater than minimal risk. The VA medical facility Director must approve participation in the proposed research that includes children (see guidance at: <http://www.research.va.gov/resources/policies/default.cfm>).

NOTE: For purposes of this Handbook, research involving biological specimens or data obtained from children is considered to be research involving children even if de-identified. If the biological specimens or data were previously collected, they must have been collected under applicable policies and ethical guidelines.

b. The IRB must have the appropriate expertise to evaluate any VA research involving children and must comply with the requirements of 45 CFR 46.401 - 46.404 and 46.408. **NOTE:** A link to these requirements is provided on the ORD Web site at: <http://www.research.va.gov/resources/policies/default.cfm>.

20. SUBJECTS LACKING DECISION-MAKING CAPACITY:

a. **Criteria for Enrollment.** Individuals who lack decision-making capacity may be enrolled in VA research where:

(1) The IRB determines that the proposed research entails:

(a) No greater than minimal risk to the subject; or

(b) Presents a greater probability of direct benefit to the subject than harm to the subject; or

(c) Greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition that is of vital importance for the understanding or amelioration of the subject's disorder or condition.

(2) In addition to satisfying the conditions above, the IRB determines that:

(a) The research cannot be performed solely with persons who possess decision-making capacity and the focus of the research is the disorder leading to the subjects' lack of decision-making capacity, whether or not the lack of decision-making itself is being evaluated (e.g., an individual who lacks decision-making capacity as the result of a stroke can participate in a study of cardiovascular effects of a stroke); **or**

(b) The subject of the research is not directly related to the subjects' lack of decision-making capacity but the investigator has presented a compelling argument for including such subjects (e.g., transmission of methicillin-resistant staphylococcus aureus infections in a nursing home where both individuals with and without decision-making capacity are affected).

b. **Determination of Capacity.** When planning to enter subjects with impaired decision-making capacity, investigators must address in the protocol how they will determine when surrogate consent (i.e., a LAR) will be required. In general, the research staff must perform or obtain and document a clinical assessment of decision-making capacity for any subject suspected of lacking decision-making capacity. However, the IRB must review and approve the plan to ensure that it is appropriate given the population and setting of the research. **NOTE:** *Individuals ruled incompetent by a court of law are considered to lack decision-making capacity.*

c. **Surrogate consent.** When the potential subject is determined to lack decision-making capacity, investigators must obtain consent from the LAR of the subject (i.e., surrogate consent). **NOTE:** *Investigators and IRBs have a responsibility to consult with the Office of General Counsel (OGC) regarding state or local requirements for surrogate consent for research that may supersede VA requirements.*

d. **Authorized Person.** The following persons are authorized to consent on behalf of persons who lack decision-making capacity in the following order of priority in accordance with VA regulations at 38 CFR 17.32(e), (g)(3). **NOTE:** *Consent for research is required in addition to the consent that is obtained for the patient's non-research related treatments and procedures.*

(1) Health care agent (i.e., an individual named by the subject in a Durable Power of Attorney for Health Care);

(2) Legal guardian or special guardian;

(3) Next of kin: a close relative of the patient 18 years of age or older, in the following priority: spouse, child, parent, sibling, grandparent, or grandchild; or

(4) Close friend.

NOTE: *The persons authorized to consent on behalf of persons who lack decision-making capacity for participation in the research may not necessarily be the same as the persons authorized to provide permission for the use and disclosure of information on a HIPAA authorization on behalf of persons who lack decision-making capacity (see VHA Handbook 1605.1).*

e. **Dissent or Assent.** If feasible, the investigator must explain the proposed research to the prospective research subject even when the surrogate gives consent. Although unable to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may a subject be forced or coerced to participate in a research study even if the LAR has provided consent.

f. **Responsibilities of LARs.** LARs are acting on behalf of the potential subjects, therefore:

(1) LARs must be told that their obligation is to try to determine what the subjects would do if able to make an informed decision.

(2) If the potential subjects' wishes cannot be determined, the LARs must be told they are responsible for determining what is in the subjects' best interest.

21. CERTIFICATES OF CONFIDENTIALITY:

a. Several HHS operating agencies issue Certificates of Confidentiality to protect research subjects. Generally, any research project that collects personally identifiable, sensitive information and that has been approved by an IRB operating under either an approved FWA issued by the OHRP or the approval of the FDA is eligible for a Certificate of Confidentiality. Sensitive information for purposes of a Certificate of Confidentiality includes (but is not limited to) information relating to sexual attitudes, preferences, or practices; information relating to the use of alcohol, drugs, or other addictive products; information pertaining to illegal conduct; information that, if released, might be damaging to an individual's financial standing, employability, or reputation within the community or might lead to social stigmatization or discrimination; information pertaining to an individual's psychological well-being or mental health; and genetic information or tissue samples.

b. Some types of research projects that are eligible for a Certificate of Confidentiality include:

(1) Research on HIV, Acquired Immune Deficiency Syndrome, and other sexually transmitted diseases;

(2) Studies that collect information on sexual attitudes, preferences, or practices;

(3) Studies on the use of alcohol, drugs, or other addictive products;

(4) Studies that collect information on illegal conduct;

(5) Studies that gather information that if released could be damaging to a participant's financial standing, employability, or reputation within the community;

(6) Research involving information that might lead to social stigmatization or discrimination if it were disclosed;

(7) Research on participants' psychological well-being or mental health;

(8) Genetic studies, including those that collect and store biological samples for future use; and

(9) Research on behavioral interventions and epidemiologic studies.

c. Investigators and IRBs are urged to consider the use of Certificates of Confidentiality when appropriate.

d. When VA conducts a study that is protected by a Certificate of Confidentiality, the following health record documentation provisions apply:

(1) For studies that do not involve a medical intervention (e.g., observational studies, including interview and questionnaire studies), no annotation may be made in the health record.

(2) For studies that involve a medical intervention, a progress note entry should indicate that an individual has been enrolled in a research study, any details that would affect the subject's clinical care, and the name and contact information for the investigator conducting the study. Subjects' informed consent forms and HIPAA authorization documents are not to be included in the health record.

e. Investigators should work with the research office in their facility to assure that when Veterans are enrolled in a study protected by a Certificate of Confidentiality, they are not simultaneously enrolled in other interventional studies unless it is absolutely clear that this enrollment does not raise safety issues.

22. PRIVACY OFFICER AND INFORMATION SECURITY OFFICER DUTIES: The PO and the ISO serve in an advisory capacity to the IRB as either non-voting members or as consultants. The facility PO and ISO are responsible for:

a. Ensuring that the proposed research complies with all applicable local, VA, and other Federal requirements for privacy and confidentiality, and for information security, by identifying and addressing potential concerns about proposed research studies.

b. Reviewing the proposed study protocol, study specific privacy and security information, and any other relevant materials submitted with the IRB application.

c. Identifying deficiencies in the provisions for privacy and confidentiality or information security, respectively, of the proposed research, and making recommendations to the investigator and/or the IRB of options available to correct the deficiencies.

d. Following up with the investigator and/or the IRB, in a timely manner, to ensure the proposed research is in compliance with relevant privacy and confidentiality and information security requirements, respectively, before the investigator initiates the study.

e. A final review is required only after the IRB has approved the study to ensure no further changes impact the privacy and security requirements of this study.

NOTE: *If a study includes information covered under 38 U.S.C. 7332 that will be disclosed outside of VA, the study must include written assurance from the VA researcher, e.g. within the protocol, that the purpose of the data is to conduct scientific research and that no personnel involved in the study will identify, directly or indirectly, any individual patient or subject in any report of such research, e.g. manuscript or publication.*

23. HIPAA AUTHORIZATION:

a. **Written Authorization.** In accordance with the HIPAA Privacy Rule at 45 CFR 164.508, a written authorization signed by the individual to whom the information or record pertains, is required when VA medical facilities need to access, collect, develop, use, or disclose individually-identifiable health information for a purpose other than treatment, payment, or health care operations (e.g., research) unless there is legal authority (e.g., waiver, limited data set with data use agreement, etc.) to disclose such information (see VHA Handbook 1605.1).

(1) VA Form 10-0493, Authorization for Use & Release of Individually Identifiable Health Information for VHA Research, must be used to document the authorization. The authorization may not be embedded in the consent form;

(2) The information in the authorization must not contradict any provisions of the protocol, informed consent, or other documents submitted for IRB approval;

(3) All potential disclosures to a non-VA entity must be listed within the authorization;

(4) The IRB does not approve the authorization but does review it to ensure the consent document, protocol, and authorization are consistent;

(5) The PO must review the HIPAA authorization to ensure it contains all required elements and is consistent with all privacy requirements before the PI can begin to use or collect the individual's information based on an approved research protocol (see VHA Handbook 1605.1);

(6) Data disclosed under a properly executed HIPAA authorization must be securely transferred according to VA information security requirements;

b. **Waiver of HIPAA Authorization.** An investigator requesting a waiver of HIPAA authorization must provide information sufficient to allow the IRB to make the required determination. In accordance with the HIPAA Privacy Rule at 45 CFR 164.512(i)(2), the IRB must document the following:

(1) Identification of the IRB of Record;

(2) Date of IRB approval of waiver of HIPAA authorization;

(3) Statement that the waiver of HIPAA authorization satisfies the following criteria:

(a) The use or disclosure of the requested information involves no more than minimal risk to the privacy of individuals based on, at least, the presence of the following elements:

1. An adequate plan to protect the identifiers from improper use and disclosure;

2. An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law. **NOTE:** *Records, including identifiers, must be retained until disposition instructions are approved by the National Archives*

and Records Administration (NARA) and are published in VHA RCS 10-1. Once the disposition schedule is determined, records should be disposed in accordance with VHA RCS 10-1; and

3. Adequate written assurances that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the requested information is permitted by the Privacy Rule;

(b) The research could not practicably be conducted without the waiver; and

(c) The research could not practicably be conducted without access to and use of the requested information.

(4) A brief description of the PHI for which the IRB has determined use or disclosure to be necessary.

(5) Identification of the IRB review procedure used to approve the waiver of HIPAA authorization (either convened IRB review procedures or expedited review procedures).

(6) Signature of the Chair of the IRB, or a qualified voting member of the IRB designated by the Chair, on the HIPAA authorization waiver document. **NOTE:** Signatures may be electronic if they meet VA requirements for electronic signatures.

NOTE: If the IRB does not document the waiver of authorization as required, the waiver is not valid. If the IRB of record cannot provide a waiver of authorization, a properly constituted Privacy Board may be used to review and approve the waiver request in accordance with 45 CFR 164.512(i) (see VHA Handbook 1605.1).

c. **Activities Preparatory to Research.** VA investigators may use individually-identifiable health information to prepare a research protocol prior to submission of the protocol to the IRB for approval without obtaining a HIPAA authorization or waiver of authorization.

(1) VA investigators must not arbitrarily review PHI based on their employee access to PHI until the investigator documents the following required information as “Preparatory to Research” in a designated file that is readily accessible for those required to audit such information (e.g., Health Information Manager or PO):

(a) Access to PHI is only to prepare a protocol;

(b) No PHI will be removed from the covered entity (i.e., VHA); and

(c) Access to PHI is necessary for preparation of the research protocol.

(2) Non-VA researchers may not obtain VA information for preparatory to research activities without appropriate VA approvals (see VHA Handbook 1605.1).

(3) During the preparatory to research activities the VA investigator:

(a) Must only record aggregate data. The aggregate data may only be used for background information to justify the research or to show that there are adequate numbers of potential subjects to allow the investigator to meet enrollment requirements for the research study;

(b) Must not record any individually identifiable health information; and

(c) Must not use any individually identifiable information to recruit research subjects.

NOTE: *Preparatory activities can include reviewing database output (computer file or printout) containing identifiable health information generated by the database owner, if the investigator returns the database output to the database owner when finished aggregating the information.*

(4) Contacting potential research subjects and conducting pilot or feasibility studies are not considered activities preparatory to research.

(5) Activities preparatory to research only encompass the time to prepare the protocol and ends when the protocol is submitted to the IRB.

24. PARTICIPATION OF NON-VETERANS AS RESEARCH SUBJECTS:

a. Non-Veterans may be entered into a VA-approved research study that involves VA outpatient or VA hospital treatment (38 CFR 17.45, 17.92), but only when there are insufficient Veteran patients suitable for the study. The investigator must justify including non-Veterans and the IRB must review the justification and provide specific approval for recruitment of non-Veterans.

(1) **Outpatient Care for Research Purposes.** Any person who is a bona fide volunteer may be furnished outpatient treatment when the treatment to be rendered is part of an approved VA research study and there are insufficient Veteran patients suitable for the study (38 CFR 17.92).

(2) **Hospital Care for Research Purposes.** Any person who is a bona fide volunteer may be admitted to a VA hospital when the treatment to be rendered is part of an approved VA research study and there are insufficient Veteran patients suitable for the study (38 CFR 17.45).

b. Non-Veterans may be recruited for studies that will generally benefit Veterans and their well-being but would not include Veterans as subjects. Examples include surveys of VA providers, studies involving Veterans' family members, or studies including active duty military personnel. Although active duty military personnel are not considered Veterans, they should be included in VA studies whenever appropriate.

c. In addition to the non-Veterans referenced above, active duty military personnel may be entered into VA research conducted jointly by VA and DoD or within DoD facilities.

d. All VA regulations and policies related to Veterans as research subjects apply to non-Veterans entered into VA research.

e. Non-Veterans may not be entered into VA studies simply because a non-Veteran population is easily accessible to the investigator.

f. Investigators must follow VHA Handbook 1605.04, Notice of Privacy Practices, to provide notice of privacy practices and acknowledgement for any non-Veteran enrolled in the approved protocol.

25. TREATMENT OF RESEARCH-RELATED INJURIES:

a. VA medical facilities, including joint VA-DoD federal health care centers, must provide necessary medical treatment (i.e., not just emergency treatment) to a research subject injured as a result of participation in a research study approved by a VA R&D Committee and conducted under the supervision of one or more VA employees (38 CFR 17.85). This requirement does not apply to:

- (1) Treatment for injuries due to non-compliance by a subject with study procedures; or
- (2) Research conducted for VA under a contract with an individual or a non-VA institution.

b. Care for VA research subjects under this paragraph must be provided in VA medical facilities, except in the following situations:

(1) If VA facilities are not capable of furnishing economical care or are not capable of furnishing the care or services required, VA medical facility Directors shall contract for the needed care;

(2) If inpatient care must be provided to a non-Veteran under this paragraph, VA medical facility Directors may contract for such care; or

(3) If a research subject needs treatment in a medical emergency for a condition covered by this paragraph, VA medical facility Directors must provide reasonable reimbursement for the emergency treatment in a non-VA facility.

26. INTERNATIONAL RESEARCH:

a. VA international research is defined as any VA-approved research conducted at international sites (i.e., not within the United States (U.S.), its territories, or Commonwealths), any VA-approved research using either identifiable or de-identified human biological specimens or identifiable or de-identified human data originating from international sites, or any VA-approved research that entails sending such specimens or data out of the U.S. This definition applies regardless of the funding source (funded or unfunded) and to research conducted through any mechanism of support including MOUs, CRADAs, grants, contracts, or other agreements.

NOTE: *For the purposes of this Handbook, research conducted at U.S. military bases, ships, or embassies is not considered international research.*

(1) Sending specimens or data to individuals with VA appointments at international sites (e.g., a WOC appointment, a VA investigator on sabbatical at an international site) is considered

international research. Remote use of data that is maintained on VA computers within the U.S. or Puerto Rico and accessed via a secure connection is not considered international research.

(2) International research includes multi-site trials involving non-U.S. sites where VA is the study sponsor, a VA investigator is the overall study-wide PI, VA holds the Investigational New Drug (IND), or the VA manages the data collection and the data analyses.

(3) International research does not include studies in which VA is only one of multiple participating sites where the overall study-wide PI is not a VA investigator (i.e., the PI for the study as a whole is not a VA investigator).

b. Before approving international research involving human subjects research, the IRB must ensure that human subjects outside of the U.S. who participate in research projects in which VA is a collaborator receive equivalent protections as research participants inside the U.S. (see OHRP guidance at <http://www.hhs.gov/ohrp/international/index.html>). **NOTE:** *The VA medical facility Director must approve participation in the proposed international research (see guidance at: <http://www.research.va.gov/resources/policies/default.cfm>).*

c. All international research must also be approved explicitly in a document signed by the VA medical facility Director, except for Cooperative Studies Program activities which must be approved by the CRADO.

27. ACCREDITATION OF HUMAN RESEARCH PROTECTION PROGRAMS: Any VA facility with a FWA must obtain accreditation of its HRPP by the accrediting organization specified by ORD. This HRPP accreditation must be obtained in accordance with a schedule determined by ORD based on the facility's HRPP accreditation status and history. **NOTE:** *Refer to the ORD Web site for details on accreditation procedures: <http://www.research.va.gov/pride/accreditation/default.cfm>.*

a. Maintenance of HRPP accreditation must be in accordance with ORD HRPP accreditation requirements including those relating to academic affiliates or other Federal agencies providing IRB services to the VA facility.

b. Academic affiliates may be required to cooperate with the accrediting organization specified by ORD or to maintain their own accreditation with another accrediting organization recognized by ORD.

28. STUDENT AND OTHER TRAINEE RESEARCH:

a. Trainees (e.g., students, residents, or fellows of any profession) may serve as participants, but not PIs within a VA facility, use VA human subjects data, or use human biological specimens that have been collected within VA for clinical, administrative, or research purposes only when:

(1) The study has been approved by the local VA medical facility and IRB, if appropriate; and

(2) Either they are:

(a) Enrolled in an institution with an educational affiliation agreement with that VA facility;
or

(b) Directly appointed to a VA training program that has no external institutional sponsorship (e.g. VA Advanced Fellowship). **NOTE:** *A waiver may be obtained from the CRADO under special circumstances.*

b. A VA investigator sufficiently experienced in the area of the trainee's research interest must serve as PI and is responsible for oversight of the research and the trainee/student. The PI is responsible for ensuring the trainee/student complies with all applicable local, VA and other federal requirements including those related to research, information security, and privacy.

(1) If the trainee does not complete all aspects of the research prior to leaving VA, the VA investigator must ensure the protocol is completed or terminated in an orderly fashion, and in accordance with all applicable local, VA, and other federal requirements.

(2) When the trainee leaves VA, the VA investigator is responsible for ensuring that all research records are retained by VA.

29. VA INVESTIGATOR RESPONSIBILITIES: The investigator must give first priority to the protection of research subjects, uphold professional and ethical standards and practices, and adhere to all applicable VA and other federal requirements, including the local VA facility's policies and procedures, regarding the conduct of research and the protection of human subjects. The investigator must hold a current VA appointment to conduct VA research.

a. **Qualifications to Conduct Human Subjects Research.** VA investigators must have the appropriate training, education, expertise, and credentials to conduct the research according to the research protocol.

(1) PIs must ensure that all research staff are qualified (e.g., including but not limited to appropriate training, education, expertise, and credentials) to perform procedures assigned to them during the course of the study.

(2) Investigators and their staff conducting human subjects research must be credentialed and privileged as required by current local and VA requirements (see VHA Handbook 1100.19 and VHA Directive 2012-030, Credentialing of Health Care Professionals, or successor policy). Investigators and their research staff may only perform those activities in a research study for which they have the relevant credentials and privileges.

(3) Investigators and co-investigators must be identified on the IRB application and must provide credentials, conflict of interest statements or other documentation required by VA and local facility policies.

(4) All individuals involved in conducting VA human subjects research are required to complete training in ethical principles on which human subjects research is to be conducted. Specific requirements regarding the type and frequency of training are found on ORD's Web site at: <http://www.research.va.gov/pride/training/options.cfm>. All other applicable VA and VHA

training requirements at the local and national level must be met (e.g., privacy and information security training).

b. **Research Protocol.** The investigator must develop and submit a research protocol that is scientifically valid, describes the research objectives, background and methodology, provides for fair and equitable recruitment and selection of subjects, minimizes risks to subjects and others, and describes a data and safety monitoring plan consistent with the nature of the study. The research must be relevant to the health or welfare of the Veteran population. When relevant, the protocol must include the following safety measures:

- (1) The type of safety information to be collected including AEs;
- (2) Frequency of safety data collection;
- (3) Frequency or periodicity of review of cumulative safety data;
- (4) Statistical tests for analyzing the safety data to determine if harm is occurring; and
- (5) Conditions that trigger an immediate suspension of the research, if applicable.

c. **Approvals.** The investigator must submit the protocol for initial review and obtain written approvals from the IRB, other applicable committees, and from the R&D Committee. In addition, the investigator must receive written notice from the ACOS/R&D that the research may commence before initiating the research.

(1) Once approved by the IRB, the protocol must be implemented as approved. All modifications to the approved research protocol or consent form must be approved by the IRB prior to initiating the changes except when necessary to eliminate apparent immediate hazards to the subject.

(2) The investigator must also obtain continuing review and approval at a frequency established by the IRB, but not less than once every year and is expected to submit all materials required for continuing review in sufficient time to assure approval prior to the expiration date. No research activities may be conducted at any time without a currently valid IRB approval.

d. **Conflict Of Interest.** The investigator must disclose to the IRB any potential, actual, apparent, or perceived conflict of interest of a financial, professional, or personal nature that may affect any aspect of the research, and comply with all applicable VA and other federal requirements regarding conflict of interest.

e. **Initial Contact.** During the recruitment process, members of the research team must make initial contact with potential subjects in person or by letter prior to initiating any telephone contact, unless there is written documentation that the subject is willing to be contacted by telephone about the study in question or a specific kind of research as outlined in the study.
***NOTE:** If a research repository from a previous study is used to identify subjects, there must be an IRB approved HIPAA waiver for this activity in the new protocol.*

(1) Any initial contact by letter or telephone must provide a telephone number or other means that the potential subject can use to verify that the study constitutes VA research.

(2) If a contractor makes the initial contact by letter, the VA investigator must sign the letter.

NOTE: *This paragraph does not apply to situations where a Veteran calls in response to an advertisement.*

f. **Informed Consent for Research.** The investigator must obtain and document legally effective informed consent of the subject or the subject's LAR prospectively (i.e., no screening or other interaction or intervention involving a human subject can occur until after the IRB-approved informed consent requirements have been met) that is in alignment with ethical principles that govern informed consent for research. The only exceptions are if the IRB determines the research is exempt, or approves a waiver of the informed consent process, or approves a waiver of the signed informed consent document (see paragraphs 15 and 16).

(1) If the investigator does not personally obtain informed consent, the investigator must delegate this responsibility in writing (e.g., by use of a delegation letter) to research staff sufficiently knowledgeable about the protocol and related concerns to answer questions from prospective subjects, and about the ethical basis of the informed consent process and protocol.

(a) If the investigator contracts with a firm, e.g., a survey research firm, to obtain consent from subjects, collect private individually identifiable information from human subjects, or are involved in activities that would institutionally engage the firm in human subjects research, the firm must have its own IRB oversight of the activity. In addition, the PO must determine that there is appropriate authority to allow the disclosure of individual names and other information to the contracted firm.

(b) The investigator must ensure that all original signed and dated informed consent documents are maintained in the investigator's research files, readily retrievable, and secure.

g. **HIPAA Authorization.** The investigator or designee must obtain HIPAA authorization for the use and disclosure of the subject's PHI, or obtain an IRB-approved waiver of HIPAA authorization (see paragraph 23 in this Handbook and VHA Handbook 1605.1) unless there is a limited data set and appropriate DUA.

h. **Reporting.** The investigator is responsible for reporting unanticipated problems involving risks to subjects or others, serious unanticipated problems involving risks to subjects or others, local unanticipated serious adverse events, apparent serious or continuing noncompliance, any termination or suspension of research; and privacy or information security incidents related to VA research, including: any inappropriate access, loss, or theft of PHI; noncompliant storage, transmission, removal, or destruction of PHI; or theft, loss, or noncompliant destruction of equipment containing PHI, in accordance with local facility or IRB SOPs and VHA Handbook 1058.01. **NOTE:** *Current guidance on such reporting can be found on the ORO Web site at: <http://vawww.vha.vaco.portal.va.gov/sites/ORO/RCO/Memoranda%20and%20Clarifications/Forms/AllItems.aspx>. This is an internal VA Web site not available to the public.*

i. **Research Records.** All written information given to subjects must be in the investigator's research file along with the consent form(s). The investigator's research records are not yet scheduled in VHA RCS 10-1 and therefore must be retained until disposition instructions, as approved by NARA, are published in VHA RCS 10-1. ***NOTE: Once the disposition schedule is determined, records should be disposed in accordance with VHA RCS 10-1. If the investigator leaves VA, all research records must be retained by the VA facility where the research was conducted.***

j. **VHA Health Record.** A VHA health record must be created or updated, and a progress note created, for all research subjects (Veterans or Non-Veterans) who are admitted to VA medical facilities as in-patients, treated as outpatients at VA medical facilities, or when research procedures or interventions are used in or may impact the medical care of the research subject at a VA medical facility or at facilities contracted by VA to provide services to Veterans (e.g., Community-Based Outpatient Clinics or nursing homes) (see VHA Handbook 1907.01). Informed consent documents are not required to be in the health record.

k. **Investigational Drugs and Devices.** The investigator must conduct VA human subjects research involving investigational drugs and devices in accordance with all applicable VA policies and other federal requirements including, but not limited to: this Handbook, VHA Handbook 1108.04, and applicable FDA regulations. The storage and security procedures for test articles used in research must be reviewed and approved by the IRB and follow all applicable federal rules.

l. **Initiation of Research Projects.** IRB approval is for a specified time period based on the degree of risk of the study, not to exceed 1 year. The IRB determines the expiration date based upon its date of review and communicates that date to the investigator in the written approval letter. The investigator must not initiate the IRB approved research protocol until all applicable requirements in VHA Handbook 1200.01 have also been met including obtaining R&D Committee approval.

m. **Expiration of IRB Approval.** There is no provision for any grace period to extend the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur on or before the date when IRB approval expires. If approval expires, the investigator must:

(1) Stop all research activities including, but not limited to, enrollment of new subjects, analyses of individually identifiable data, and research interventions or interactions with currently participating subjects, except where stopping such interventions or interactions could be harmful to those subjects; and

(2) Immediately submit to the IRB Chair a list of research subjects who could be harmed by stopping specified study interventions or interactions. The IRB Chair must determine within 2 business days whether or not such interventions or interactions may continue.

30. REFERENCES:

- a. 5 U.S.C. 552a, The Privacy Act of 1974.

- b. 21 U.S.C. 321-60, Federal Food, Drug, and Cosmetic Act.
- c. 38 U.S.C. 501, Rules and Regulations.
- d. 38 U.S.C. 1710, Eligibility For Hospital, Nursing Home, and Domiciliary Care.
- e. 38 U.S.C. 5701, Confidential Nature of Claims.
- f. 38 U.S.C. 5705, Confidentiality of Medical Quality-Assurance Records.
- g. 38 U.S.C. 7331, Informed Consent.
- h. 38 U.S.C. 7332, Confidentiality of Drug Abuse, Alcoholism and Alcohol Abuse, Infection with Human Immunodeficiency Virus (HIV), and Sickle Cell Anemia Medical Records.
- i. 38 U.S.C. 7334, Regulations.
- j. 42 U.S.C. 262, Regulation of Biological Products.
- k. 10 CFR Part 20, Standards for Protection Against Radiation.
- l. 10 CFR Part 35, Medical Use of Byproduct Material.
- m. 21 CFR Part 11, Electronic Records; Electronic Signatures.
- n. 21 CFR Part 50, Protection of Human Subjects.
- o. 21 CFR Part 56, IRBs.
- p. 21 CFR Part 312, Investigational New Drug Application.
- q. 21 CFR Part 812, Investigational Device Exemptions.
- r. 38 CFR Part 16, Protection of Human Subjects.
- s. 38 CFR Part 17, Medical.
- t. 45 CFR Part 46, Protection of Human Subjects, Subpart A – Basic HHS Policy for Protection of Human Subjects; Subpart B – Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research; Subpart C – Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects; and Subpart D – Additional Protections for Children Involved as Subjects in Research.
- u. 45 CFR Part 160, General Administrative Requirements.
- v. 45 CFR Part 164, Security and Privacy, Subpart E –Privacy of Individually Identifiable Health Information.

- w. Expedited Review Categories, 63 FR 60364, Nov. 9, 1998.
- x. VA Directive 6500, Managing Information Security Risk: VA Information Security Program.
- y. VHA RCS 10-1.
- z. VHA Directive 1200, VHA R&D Program.
- aa. VHA Directive 2012-030, Credentialing of Health Care Professionals.
- bb. VHA Handbook 1004.01, Informed Consent for Clinical Treatments and Procedures.
- cc. VHA Handbook 1058.01, Research Compliance Reporting Requirements.
- dd. VHA Handbook 1058.03, Assurance of Protection for Human Subjects in Research.
- ee. VHA Handbook 1058.05, VHA Operations Activities That May Constitute Research.
- ff. VHA Handbook 1100.19, Credentialing and Privileging.
- gg. VHA Handbook 1108.04, Investigational Drugs and Supplies.
- hh. VHA Handbook 1200.01, R&D Committee.
- ii. VHA Handbook 1200.08, Safety of Personnel Engaged in Research.
- jj. VHA Handbook 1200.12, Use of Data and Data Repositories in VHA Research.
- kk. VHA Handbook 1200.16, Off Site Research.
- ll. VHA Handbook 1200.17, VA NPC Authorized By Title 38 U.S.C. §§ 7361-66.
- mm. VHA Handbook 1200.2, Research Business Operations.
- nn. VHA Handbook 1605.1, Privacy and Release of Information.
- oo. VHA Handbook 1605.02, Minimum Necessary Standard for Protected Health Information.
- pp. VHA Handbook 1605.04, Notice of Privacy Practices.
- qq. VHA Handbook 1907.01, Health Information Management and Health Records.
- rr. VA Handbook 6500, Risk Management Framework for VA Information Systems - Tier 3: VA Information Security Program.

APPENDIX A

CATEGORIES OF EXEMPT RESEARCH

1. Research activities in which the only involvement of human subjects will be in one or more of the following categories may be exempt from this policy (38 CFR 16.101(b)):
 2. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:
 - a. Research on regular and special education instructional strategies; or
 - b. Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
 3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
 - a. Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
 - b. Any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.
- NOTE:** *The exemption for research involving survey or interview procedures or observations of public behavior does not apply to research involving children, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.*
4. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph 3 of this Appendix, if:
 - a. The human subjects are elected or appointed public officials or candidates for public office; or
 - b. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
 5. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
 6. Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:

APPENDIX A

- a. Public benefit or service programs;
- b. Procedures for obtaining benefits or services under those programs;
- c. Possible changes in or alternatives to those programs or procedures; or
- d. Possible changes in methods or levels of payment for benefits or services under those programs.

NOTE: *The determination of exempt status for research and demonstration projects meeting the criteria in paragraph 6 in this Appendix must be made by the Under Secretary for Health on behalf of the Secretary of VA, after consultation with Office of Research and Development (ORD), Office of Research Oversight (ORO), Office of General Counsel (OGC), and other experts, as appropriate.*

- 7. Taste and food quality evaluation and consumer acceptance studies,
 - a. If wholesome foods without additives are consumed; or
 - b. If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration (FDA) or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

APPENDIX B

ACTIVITIES APPROPRIATE FOR EXPEDITED REVIEW

Source: 63 FR 60364-60367, Nov. 9, 1998.

1. APPLICABILITY: Research activities that: (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the Institutional Review Board (IRB) through the expedited review procedure authorized by Title 45 Code of Federal Regulations (CFR) 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

- a. The categories in this list apply regardless of the age of subjects, except as noted.
- b. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
- c. The expedited review procedure may not be used for classified research involving human subjects.
- d. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--utilized by the IRB.
- e. The below research categories, 2.a. through 2.g., pertain to both initial and continuing IRB review.

2. RESEARCH CATEGORIES:

- a. Clinical studies of drugs and medical devices only when the following conditions are met:
 - (1) 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.)
 - (2) 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.
- b. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

APPENDIX B

(1) From healthy, non-pregnant 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

(2) From other adults and children (as defined under 45 CFR 46.402(a)), 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.

c. Prospective collection of biological specimens for research purposes by noninvasive means. Examples include, but are not limited to:

(1) Hair and nail clippings in a non-disfiguring manner;

(2) Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;

(3) Permanent teeth if routine patient care indicates a need for extraction;

(4) Excreta and external secretions (including sweat);

(5) 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;

(6) Placenta removed at delivery;

(7) Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;

(8) Supra- and sub-gingival 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;

(9) Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;

(10) Sputum collected after saline mist nebulization.

d. 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 include, but are not limited to:

(1) 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 subjects' privacy;

(2) Weighing or testing sensory acuity;

(3) Magnetic resonance imaging;

(4) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; and

(5) Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

e. 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.*)

f. Collection of data from voice, video, digital, or image recordings made for research purposes.

g. 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), (b)(3)). This listing refers only to research that is not exempt.*)

h. Continuing review of research previously approved by the convened IRB as follows:

(1) Where:

(a) The research is permanently closed to the enrollment of new subjects;

(b) All subjects have completed all research-related interventions; and

(c) The research remains active only for long-term follow-up of subjects; or

(2) Where no subjects have been enrolled and no additional risks have been identified; or

(3) Where the remaining research activities are limited to data analysis.

i. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where research categories 2.b. through 2.h. do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

4-drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty Analgesia in Veterans: Manual of Operating Procedures (MOP) for this Single-Site Study

21 CFR Part 50

PART 50—PROTECTION OF HUMAN SUBJECTS

Subpart B—Informed Consent of Human Subjects

Contents

- [§50.20 General requirements for informed consent.](#)
 - [§50.23 Exception from general requirements.](#)
 - [§50.24 Exception from informed consent requirements for emergency research.](#)
 - [§50.25 Elements of informed consent.](#)
 - [§50.27 Documentation of informed consent.](#)
-

SOURCE: 46 FR 8951, Jan. 27, 1981, unless otherwise noted.

[↑ Back to Top](#)

§50.20 General requirements for informed consent.

Except as provided in §§50.23 and 50.24, no investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

[46 FR 8951, Jan. 27, 1981, as amended at 64 FR 10942, Mar. 8, 1999]

[↑ Back to Top](#)

§50.23 Exception from general requirements.

(a) The obtaining of informed consent shall be deemed feasible unless, before use of the test article (except as provided in paragraph (b) of this section), both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

- (1) The human subject is confronted by a life-threatening situation necessitating the use of the test article.
- (2) Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
- (3) Time is not sufficient to obtain consent from the subject's legal representative.
- (4) There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

(b) If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the subject, and time is not sufficient to obtain the independent determination required in paragraph (a) of this section in advance of using

4-drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty Analgesia in Veterans: Manual of Operating Procedures (MOP) for this Single-Site Study

the test article, the determinations of the clinical investigator shall be made and, within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

(c) The documentation required in paragraph (a) or (b) of this section shall be submitted to the IRB within 5 working days after the use of the test article.

(d)(1) Under 10 U.S.C. 1107(f) the President may waive the prior consent requirement for the administration of an investigational new drug to a member of the armed forces in connection with the member's participation in a particular military operation. The statute specifies that only the President may waive informed consent in this connection and the President may grant such a waiver only if the President determines in writing that obtaining consent: Is not feasible; is contrary to the best interests of the military member; or is not in the interests of national security. The statute further provides that in making a determination to waive prior informed consent on the ground that it is not feasible or the ground that it is contrary to the best interests of the military members involved, the President shall apply the standards and criteria that are set forth in the relevant FDA regulations for a waiver of the prior informed consent requirements of section 505(i)(4) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)(4)). Before such a determination may be made that obtaining informed consent from military personnel prior to the use of an investigational drug (including an antibiotic or biological product) in a specific protocol under an investigational new drug application (IND) sponsored by the Department of Defense (DOD) and limited to specific military personnel involved in a particular military operation is not feasible or is contrary to the best interests of the military members involved the Secretary of Defense must first request such a determination from the President, and certify and document to the President that the following standards and criteria contained in paragraphs (d)(1) through (d)(4) of this section have been met.

(i) The extent and strength of evidence of the safety and effectiveness of the investigational new drug in relation to the medical risk that could be encountered during the military operation supports the drug's administration under an IND.

(ii) The military operation presents a substantial risk that military personnel may be subject to a chemical, biological, nuclear, or other exposure likely to produce death or serious or life-threatening injury or illness.

(iii) There is no available satisfactory alternative therapeutic or preventive treatment in relation to the intended use of the investigational new drug.

(iv) Conditioning use of the investigational new drug on the voluntary participation of each member could significantly risk the safety and health of any individual member who would decline its use, the safety of other military personnel, and the accomplishment of the military mission.

(v) A duly constituted institutional review board (IRB) established and operated in accordance with the requirements of paragraphs (d)(2) and (d)(3) of this section, responsible for review of the study, has reviewed and approved the investigational new drug protocol and the administration of the investigational new drug without informed consent. DOD's request is to include the documentation required by §56.115(a)(2) of this chapter.

(vi) DOD has explained:

(A) The context in which the investigational drug will be administered, e.g., the setting or whether it will be self-administered or it will be administered by a health professional;

(B) The nature of the disease or condition for which the preventive or therapeutic treatment is intended; and

(C) To the extent there are existing data or information available, information on conditions that could alter the effects of the investigational drug.

(vii) DOD's recordkeeping system is capable of tracking and will be used to track the proposed treatment from supplier to the individual recipient.

4-drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty Analgesia in Veterans: Manual of Operating Procedures (MOP) for this Single-Site Study

- (viii) Each member involved in the military operation will be given, prior to the administration of the investigational new drug, a specific written information sheet (including information required by 10 U.S.C. 1107(d)) concerning the investigational new drug, the risks and benefits of its use, potential side effects, and other pertinent information about the appropriate use of the product.
 - (ix) Medical records of members involved in the military operation will accurately document the receipt by members of the notification required by paragraph (d)(1)(viii) of this section.
 - (x) Medical records of members involved in the military operation will accurately document the receipt by members of any investigational new drugs in accordance with FDA regulations including part 312 of this chapter.
 - (xi) DOD will provide adequate followup to assess whether there are beneficial or adverse health consequences that result from the use of the investigational product.
 - (xii) DOD is pursuing drug development, including a time line, and marketing approval with due diligence.
 - (xiii) FDA has concluded that the investigational new drug protocol may proceed subject to a decision by the President on the informed consent waiver request.
 - (xiv) DOD will provide training to the appropriate medical personnel and potential recipients on the specific investigational new drug to be administered prior to its use.
 - (xv) DOD has stated and justified the time period for which the waiver is needed, not to exceed one year, unless separately renewed under these standards and criteria.
 - (xvi) DOD shall have a continuing obligation to report to the FDA and to the President any changed circumstances relating to these standards and criteria (including the time period referred to in paragraph (d)(1)(xv) of this section) or that otherwise might affect the determination to use an investigational new drug without informed consent.
 - (xvii) DOD is to provide public notice as soon as practicable and consistent with classification requirements through notice in the FEDERAL REGISTER describing each waiver of informed consent determination, a summary of the most updated scientific information on the products used, and other pertinent information.
 - (xviii) Use of the investigational drug without informed consent otherwise conforms with applicable law.
- (2) The duly constituted institutional review board, described in paragraph (d)(1)(v) of this section, must include at least 3 nonaffiliated members who shall not be employees or officers of the Federal Government (other than for purposes of membership on the IRB) and shall be required to obtain any necessary security clearances. This IRB shall review the proposed IND protocol at a convened meeting at which a majority of the members are present including at least one member whose primary concerns are in nonscientific areas and, if feasible, including a majority of the nonaffiliated members. The information required by §56.115(a)(2) of this chapter is to be provided to the Secretary of Defense for further review.
- (3) The duly constituted institutional review board, described in paragraph (d)(1)(v) of this section, must review and approve:
- (i) The required information sheet;
 - (ii) The adequacy of the plan to disseminate information, including distribution of the information sheet to potential recipients, on the investigational product (e.g., in forms other than written);
 - (iii) The adequacy of the information and plans for its dissemination to health care providers, including potential side effects, contraindications, potential interactions, and other pertinent considerations; and

4-drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty Analgesia in Veterans: Manual of Operating Procedures (MOP) for this Single-Site Study

(iv) An informed consent form as required by part 50 of this chapter, in those circumstances in which DOD determines that informed consent may be obtained from some or all personnel involved.

(4) DOD is to submit to FDA summaries of institutional review board meetings at which the proposed protocol has been reviewed.

(5) Nothing in these criteria or standards is intended to preempt or limit FDA's and DOD's authority or obligations under applicable statutes and regulations.

(e)(1) Obtaining informed consent for investigational in vitro diagnostic devices used to identify chemical, biological, radiological, or nuclear agents will be deemed feasible unless, before use of the test article, both the investigator (e.g., clinical laboratory director or other responsible individual) and a physician who is not otherwise participating in the clinical investigation make the determinations and later certify in writing all of the following:

(i) The human subject is confronted by a life-threatening situation necessitating the use of the investigational in vitro diagnostic device to identify a chemical, biological, radiological, or nuclear agent that would suggest a terrorism event or other public health emergency.

(ii) Informed consent cannot be obtained from the subject because:

(A) There was no reasonable way for the person directing that the specimen be collected to know, at the time the specimen was collected, that there would be a need to use the investigational in vitro diagnostic device on that subject's specimen; and

(B) Time is not sufficient to obtain consent from the subject without risking the life of the subject.

(iii) Time is not sufficient to obtain consent from the subject's legally authorized representative.

(iv) There is no cleared or approved available alternative method of diagnosis, to identify the chemical, biological, radiological, or nuclear agent that provides an equal or greater likelihood of saving the life of the subject.

(2) If use of the investigational device is, in the opinion of the investigator (e.g., clinical laboratory director or other responsible person), required to preserve the life of the subject, and time is not sufficient to obtain the independent determination required in paragraph (e)(1) of this section in advance of using the investigational device, the determinations of the investigator shall be made and, within 5 working days after the use of the device, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

(3) The investigator must submit the written certification of the determinations made by the investigator and an independent physician required in paragraph (e)(1) or (e)(2) of this section to the IRB and FDA within 5 working days after the use of the device.

(4) An investigator must disclose the investigational status of the in vitro diagnostic device and what is known about the performance characteristics of the device in the report to the subject's health care provider and in any report to public health authorities. The investigator must provide the IRB with the information required in §50.25 (except for the information described in §50.25(a)(8)) and the procedures that will be used to provide this information to each subject or the subject's legally authorized representative at the time the test results are provided to the subject's health care provider and public health authorities.

(5) The IRB is responsible for ensuring the adequacy of the information required in section 50.25 (except for the information described in §50.25(a)(8)) and for ensuring that procedures are in place to provide this information to each subject or the subject's legally authorized representative.

(6) No State or political subdivision of a State may establish or continue in effect any law, rule, regulation or other requirement that informed consent be obtained before an investigational in vitro diagnostic device may be used to identify

4-drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty Analgesia in Veterans: Manual of Operating Procedures (MOP) for this Single-Site Study

chemical, biological, radiological, or nuclear agent in suspected terrorism events and other potential public health emergencies that is different from, or in addition to, the requirements of this regulation.

[46 FR 8951, Jan. 27, 1981, as amended at 55 FR 52817, Dec. 21, 1990; 64 FR 399, Jan. 5, 1999; 64 FR 54188, Oct. 5, 1999; 71 FR 32833, June 7, 2006; 76 FR 36993, June 24, 2011]

[↑ Back to Top](#)

§50.24 Exception from informed consent requirements for emergency research.

(a) The IRB responsible for the review, approval, and continuing review of the clinical investigation described in this section may approve that investigation without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:

(1) The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

(2) Obtaining informed consent is not feasible because:

(i) The subjects will not be able to give their informed consent as a result of their medical condition;

(ii) The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and

(iii) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

(3) Participation in the research holds out the prospect of direct benefit to the subjects because:

(i) Subjects are facing a life-threatening situation that necessitates intervention;

(ii) Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and

(iii) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

(4) The clinical investigation could not practicably be carried out without the waiver.

(5) The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

(6) The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with §50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed

4-drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty Analgesia in Veterans: Manual of Operating Procedures (MOP) for this Single-Site Study

and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with paragraph (a)(7)(v) of this section.

(7) Additional protections of the rights and welfare of the subjects will be provided, including, at least:

(i) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;

(ii) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;

(iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;

(iv) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and

(v) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

(b) The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.

(c) The IRB determinations required by paragraph (a) of this section and the documentation required by paragraph (e) of this section are to be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA in accordance with §56.115(b) of this chapter.

(d) Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under §§312.30 or 812.35 of this chapter.

(e) If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under paragraph (a) of this section or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially

4-drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty Analgesia in Veterans: Manual of Operating Procedures (MOP) for this Single-Site Study

equivalent clinical investigation of the sponsor, and to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

[61 FR 51528, Oct. 2, 1996]

[↑ Back to Top](#)

§50.25 Elements of informed consent.

(a) *Basic elements of informed consent.* In seeking informed consent, the following information shall be provided to each subject:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.

(2) A description of any reasonably foreseeable risks or discomforts to the subject.

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research.

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records.

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

(8) A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(b) *Additional elements of informed consent.* When appropriate, one or more of the following elements of information shall also be provided to each subject:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

(3) Any additional costs to the subject that may result from participation in the research.

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.

4-drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty Analgesia in Veterans: Manual of Operating Procedures (MOP) for this Single-Site Study

(6) The approximate number of subjects involved in the study.

(c) When seeking informed consent for applicable clinical trials, as defined in 42 U.S.C. 282(j)(1)(A), the following statement shall be provided to each clinical trial subject in informed consent documents and processes. This will notify the clinical trial subject that clinical trial information has been or will be submitted for inclusion in the clinical trial registry databank under paragraph (j) of section 402 of the Public Health Service Act. The statement is: "A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

(d) The informed consent requirements in these regulations are not intended to preempt any applicable Federal, State, or local laws which require additional information to be disclosed for informed consent to be legally effective.

(e) Nothing in these regulations is intended to limit the authority of a physician to provide emergency medical care to the extent the physician is permitted to do so under applicable Federal, State, or local law.

[46 FR 8951, Jan. 27, 1981, as amended at 76 FR 270, Jan. 4, 2011]

 [Back to Top](#)

§50.27 Documentation of informed consent.

(a) Except as provided in §56.109(c), informed consent shall be documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent. A copy shall be given to the person signing the form.

(b) Except as provided in §56.109(c), the consent form may be either of the following:

(1) A written consent document that embodies the elements of informed consent required by §50.25. This form may be read to the subject or the subject's legally authorized representative, but, in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed.

(2) A *short form* written consent document stating that the elements of informed consent required by §50.25 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining the consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative in addition to a copy of the short form.

[46 FR 8951, Jan. 27, 1981, as amended at 61 FR 57280, Nov. 5, 1996]

**4-drug Nerve Block versus Plain Local Anesthetic
for Knee and Hip Arthroplasty Analgesia in Veterans:
Manual of Operating Procedures (MOP) for this Single-Site Study**



**Investigational Drug Study
TREATMENT ALLOCATION REQUEST
FORM**

Subject Name: _____

Initial+Last 4 digits SS# _____

Nerve Block Study

Title: 4-Drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty
Analgesia in Veterans

PRO# 1357

Principal Investigator: Brian Williams, MD

Co-Investigators: Michael Mangione, MD; Visala Muluk, MD; James Ibinson, MD

Study Coordinator: Karen Gilbert

☐ NKA OR Allergies: _____

TYPE of PROCEDURE

☐ Total KNEE replacement

☐ Total HIP Replacement

AGE

☐ ≤ 69 years old

☐ > 69 years old
maximum of 85 years

DIABETES STATUS

☐ Diabetes PRESENT

☐ Diabetes ABSENT

Randomization Number _____

Treatment Allocation Request Submitted by:

Signature _____

DATE _____

Printed Name _____

IDS USE ONLY

Envelope (Randomization) Number provided _____

Treatment allocated:

☐ CONTROL: Bupivacaine ONLY

☐ ACTIVE: BUPIVACAINE-CLONIDINE-BUPRENORPHINE-DEXAMETHASONE

Provided by: _____

DATE _____

TKA/THA NERVE BLOCK STUDY			
Form AE	Adverse Event Log	Final 02/25/2016	
Study ID _____ Staff Initials _____ Form Date (see Report Dates, below)			

Date of onset (mm/dd/yy)	Date reported to staff (mm/dd/yyyy)	Severity 1=mild 2=moderate 3=severe 4=life threatening		Serious	Expected	Related to study drug 1=unrelated 2=possibly related 3=probably related				Date reported to IRB (mm/dd/yyyy)	Outcome status 1=resolved 2=controlled/stable 3=continuing	Outcome date (mm/dd/yy) (if not continuing)	Reviewed Initials & Date
		Initial	Most severe			BPV	Clon	Bupre	DXMS				
___/___/___	___/___/___			Y N	Y N					___/___/___		___/___/___	
Description:													
___/___/___	___/___/___			Y N	Y N					___/___/___		___/___/___	
Description:													
___/___/___	___/___/___			Y N	Y N					___/___/___		/ /	
Description:													
___/___/___	___/___/___			Y N	Y N					___/___/___		___/___/___	
Description:													
___/___/___	___/___/___			Y N	Y N					___/___/___		___/___/___	
Description:													
___/___/___	___/___/___			Y N	Y N					___/___/___		___/___/___	
Description:													

BPV: bupivacaine; Clon: clonidine; Bupre: buprenorphine; DXMS: dexamethasone

TKA/THA NERVE BLOCK STUDY

Form ANES

Surgical Anesthesia and Recovery Room

Final 08/02/2016

Study ID _____

Staff Initials ____

Form Date ____ / ____ / ____

1. Date of surgery ____ / ____ / ____ (mm/dd/yy)

2. Patient weight ____ kg BMI: ____ . ____ kg/m²

3. Involved knee/hip ☐ Left ☐ Right

3.1 If of childbearing potential, pregnancy test administered.

☐ Yes ☐ No

3.2 If administered, pregnancy test result.

☐ Positive ☐ Negative

Positive pregnancy test result necessitates exclusion from trial.

4. Antiemetic prophylaxis with perphenazine 8 mg po before surgery

☐ Yes ☐ No

5. Ondansetron 4 mg IV at the end of surgery.

☐ Yes ☐ No

6. Other oral premedication with dextromethorphan 60 mg and omeprazole 20 mg

☐ Yes ☐ No

7. Antiemetic prophylaxis with aprepitant po for patients at higher PONV risk

☐ Yes ☐ No

8. Spinal anesthesia: 24-25 G pencil-point needle through 20 G introducer; hypobaric bupivacaine 12-15 mg (plain), diluted with sterile water; and clonidine 0-15 mcg

☐ Yes ☐ No ☐ N/A

If Yes, provide volume / dose and time

8.1 Spinal bupivacaine vol. ____ . ____ mL Time (mil): _____

8.2 Clonidine dose ____ mcg Time (mil): _____

9. Pre-block / pre-spinal sedation limited to one or more of these:

☐ Yes ☐ No

midazolam 4 mg fentanyl 100 mcg dexmedetomidine (max 40 mcg)

Regardless of Yes or No, specify doses used. Enter "0" (zero) if not used.

9.1 midazolam dose ____ . ____ mg

9.2 fentanyl dose ____ mcg

9.3 dexmedetomidine dose ____ mcg

9.4 other sedation ____ mg

of _____

10. Intraoperative sedation with propofol and 0.5 mg/kg ketamine

☐ Yes ☐ No

If Yes, provide dose

10.1 total ketamine dose ____ mg

11. Intraoperative conversion from RegA to GETA, with use of volatile agent and/or fentanyl during GETA?

☐ Yes ☐ No

(if volatile agent or fentanyl, then withdraw)

12. Nerve blocks performed (provide info for all that apply) mA msec End Time (military)

Lumbar plexus _____ : _____

Parasacral _____ : _____

Sciatic _____ : _____

Femoral nerve _____ : _____

☐ US-Guided

☐ US-Guided

TKA/THA NERVE BLOCK STUDY

Form ANES

Surgical Anesthesia and Recovery Room

Final 08/02/2016

Study ID _____

Staff Initials ____

Form Date ____ / ____ / ____

13. PACU Arrival (military time): _____

14. WAKE score upon PACU Arrival: _____

15. Pain score (movement) upon PACU Arrival (0-10) _____

16. PACU opioids

☐ Yes ☐ No

16a. If yes: _____
(drug(s), dose(s), route)

16b. If yes, time of first PACU opioid (military time): _____

17. When WAKE Score eligible for PACU discharge (military time): _____

18. WAKE Score when eligible for PACU discharge: _____

19. Pain score (movement) upon WAKE Score eligible for PACU discharge: _____

20. PACU time until WAKE Score eligible for discharge: _____ minutes

21. Actual PACU discharge (military time): _____

22. Total PACU time: _____ minutes

23. Source documents verified and printed?

☐ Anesthesia record (from PICIS)

☐ Pre/Post anesthesia note (from CPRS)

☐ Nerve block note; addendum to Pre-anesthesia note

☐ Spinal note; addendum to Pre-anesthesia note

☐ CPRS Post-anesthesia note

☐ PACU record (from PICIS)

TKA/THA NERVE BLOCK STUDY

Form CIRS	Cumulative Illness Rating Scale/Comorbidity	Final 08/19/2016
Study ID _____	Staff Initials ____	Form Date ____ / ____ / ____

Visit: ☐ Baseline*

Each system is rated as follows:		
1=	NONE:	No impairment to that organ/system.
2=	MILD:	Impairment does not interfere with normal activity; treatment may or may not be required; prognosis is excellent. (Examples could be skin lesions, hernias, or hemorrhoids)
3=	MODERATE:	Impairment interferes with normal activity; treatment is needed; prognosis is good. (Examples could be gallstones, diabetes, or fractures)
4=	SEVERE:	Impairment is disabling; treatment is urgently needed; prognosis is guarded. (Examples could be carcinoma, pulmonary emphysema, or congestive heart failure)
5=	EXTREMELY SEVERE:	Impairment is life threatening; treatment is urgent or of an avail; prognosis is grave. (Examples could be myocardial infarction, cerebrovascular accident, gastrointestinal bleeding, or embolus)

	None	Mild	Moderate	Severe	Extremely Severe
1. Cardiac (heart only)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
2. Hypertension (rating based on severity; affected systems are rated separately)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
3. Vascular (blood, blood vessels and cells, marrow, spleen, lymphatics)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
4. Respiratory (lungs, bronchi, trachea below the larynx)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
5. EENT (eyes, ear, nose, throat, larynx)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
6. Upper GI (esophagus, stomach, duodenum, biliary and pancreatic trees; do not include diabetes)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
7. Lower GI (intestines, hernias)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
8. Hepatic (liver only)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
9. Renal (kidneys only)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
10. Other GU (ureters, bladder, urethra, prostate, genitals)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
11. Musculoskeletal-Integumentary (muscles, bone, skin)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
12. Neurological (brain, spinal cord, nerves: do not include dementia)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
13. Endocrine-Metabolic (includes diabetes, diffuse infections, infections, toxicity)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
14. Psychiatric/Behavioral (includes dementia, depression, anxiety, agitation, psychosis)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

*Baseline: Source documents verified and printed from CPRS

☐ IMPACT RN note

☐ IMPACT NP/MD note

☐ Associated addendum

TKA/THA NERVE BLOCK STUDY			
Form CEX	Clinical Exam Form		Version 06/03/2016
Study ID _____	PT Initials _____	Data Entry Initials _____	Form Date ____/____/____

Visit: ☐ Baseline ☐ Post-op 1 ☐ Post-op 2 ☐ Post-op 3 ☐ Post-op 4 ☐ Post-op 5 ☐ Week 6

☐ Morning	☐ Morning	☐ Morning	☐ Morning	☐ Morning
☐ Afternoon	☐ Afternoon	☐ Afternoon	☐ Afternoon	☐ Afternoon
	☐ Discharge	☐ Discharge	☐ Discharge	☐ Discharge

☐ Treatment was cancelled or deferred (*all post-op days*). Number of Attempts: _____ Time: _____

Reason (check all that apply):

☐ Patient refused
☐ Test/ procedure: _____
☐ Dialysis
☐ Medical order(s): _____
☐ Ill

☐ Nursing advisement: _____
☐ Not in room/ off of ward
☐ Not appropriate for treatment because: _____
☐ With other healthcare professional: _____
☐ Preparing for discharge to: _____

☐ CPRS source document printed

☐ Treatment was attempted: (*all post-op days*)

PT Start Time: _____

Surgical side (*all form time points*): ☐ Left ☐ Right

Pain at rest - 0 to 10 (*all form time points*): _____

TKA/THA NERVE BLOCK STUDY			
Form CEX	Clinical Exam Form	Version 06/03/2016	
Study ID _____	PT Initials _____	Data Entry Initials _____	Form Date ____/____/____

NON – Surgical	Surgical
SENSATION / LIGHT TOUCH -supine position (all form time points)	
L2-L4* Distribution: Test was attempted: ☐ No ☐ Yes	L2-L4* Distribution: Test was attempted: ☐ No ☐ Yes
☐ Normal ☐ Diminished/Absent	☐ Normal ☐ Diminished/Absent
<i>*Anterior thigh and medial anterior lower leg.</i>	
L4-S3** Distribution: Test was attempted: ☐ No ☐ Yes	L4-S3** Distribution: Test was attempted: ☐ No ☐ Yes
☐ Normal ☐ Diminished/Absent	☐ Normal ☐ Diminished/Absent
<i>**Lateral lower leg and foot.</i>	
ROM - supine position (all form time points)	
☐ S/P HIP REPLACEMENT	
Test was attempted: ☐ No ☐ Yes	Test was attempted: ☐ No ☐ Yes
AROM Hip Flexion (limit to 90°): _____°	AROM Hip Flexion (limit to 90°): _____°
PROM Hip Flexion (limit to 90°): _____°	PROM Hip Flexion (limit to 90°): _____°
AROM Hip Abduction: _____°	AROM Hip Abduction: _____°
PROM Hip Abduction: _____°	PROM Hip Abduction: _____°
Pain (0 - 10): _____	Pain (0 - 10): _____
☐ S/P KNEE REPLACEMENT	
Test was attempted: ☐ No ☐ Yes	Test was attempted: ☐ No ☐ Yes
	☐ Surgeon ordered a knee flexion restriction of _____°
AROM Knee Flexion: _____°	AROM Knee Flexion: _____°
PROM Knee Flexion: _____°	PROM Knee Flexion: _____°
AROM Knee Extension*: _____°	AROM Knee Extension*: _____°
PROM Knee Extension*: _____°	PROM Knee Extension*: _____°
<i>* Flexion Contracture = negative value. Hyperextension = positive value.</i>	
Pain (0 - 10): _____	Pain 0 - 10): _____
STRAIGHT LEG RAISE (all form time points)	
Test was attempted: ☐ No ☐ Yes	Test was attempted: ☐ No ☐ Yes
Patient can raise the leg at least 20°: ☐ Yes ☐ No	Patient can raise the leg at least 20°: ☐ Yes ☐ No
Knee extension lag (≥ 5° threshold): ☐ Yes ☐ No	Knee extension lag (≥ 5° threshold): ☐ Yes ☐ No

☐ PT out of bed was attempted. (all post-op days)

☐ PT out of bed was NOT attempted. (all post-op days)

STANDING Blood Pressure (all form time points): Systolic: _____ Diastolic: _____

TKA/THA NERVE BLOCK STUDY

Form CEX

Clinical Exam Form

Version 06/03/2016

Study ID _____ PT Initials _____ Data Entry Initials _____ Form Date ____/____/____

STANDING BALANCE TESTS *(all form time points)*

The participant must be able to stand unassisted without the use of a cane or walker.

1. Side-by-Side Score *pbsbs*

Held for 10 sec

☐ 1

Proceed to Semi-Tandem Stand

Not held for 10 sec

☐ 2

Go to question #2

Not attempted *(test is complete)*

☐ 3

Go to question #3

2. Number of seconds held if less than 10 sec: . (seconds)
pbsbsles

3. If participant did not attempt test: (Mark X for reason) *pbsbsnot*

a. Tried but unable

☐ 1

b. Participant could not hold position unassisted

☐ 2

c. Not attempted, you felt unsafe

☐ 3

d. Not attempted, participant felt unsafe

☐ 4

e. Participant unable to understand instructions

☐ 5

f. Other (specify) _____ *bsbspfy*

☐ 6

g. Participant refused

☐ 998

1. Semi-Tandem Stand Score *pbsts*

Held for 10 sec

☐ 1

Proceed to Tandem Stand

Not held for 10 sec

☐ 2

Go to question #2

Not attempted *(test is complete)*

☐ 3

Go to question #3

2. Number of seconds held if less than 10 sec: . (seconds)
pbstsles

3. If participant did not attempt test: (Mark X for reason) *pbstsnot*

a. Tried but unable

☐ 1

b. Participant could not hold position unassisted

☐ 2

c. Not attempted, you felt unsafe

☐ 3

d. Not attempted, participant felt unsafe

☐ 4

TKA/THA NERVE BLOCK STUDY			
Form CEX	Clinical Exam Form	Version 06/03/2016	
Study ID _____	PT Initials _____	Data Entry Initials _____	Form Date ____/____/____

e. Participant unable to understand instructions	☐ 5
f. Other (specify) _____ <i>pbstspfy</i>	☐ 6
g. Participant refused	☐ 998

1. Tandem Stand Score <i>pbts</i>		
Held for 10 sec	☐ 1	Proceed to Next Test
Held for 3 to 9.99 sec	☐ 2	Go to question #2
Held for < than 3 sec	☐ 3	Go to question #2
Not attempted (test is complete)	☐ 4	Go to question #3
2. Number of seconds held if less than 10 sec: . (seconds) <i>pbtsless</i>		
3. If participant did not attempt test: (Mark X for reason) <i>pbtsnot</i>		
a. Tried but unable	☐ 1	
b. Participant could not hold position unassisted	☐ 2	
c. Not attempted, you felt unsafe	☐ 3	
d. Not attempted, participant felt unsafe	☐ 4	
e. Participant unable to understand instructions	☐ 5	
f. Other (specify) _____ <i>pbtsspfy</i>	☐ 6	
g. Participant refused	☐ 998	

GAIT SPEED *(all form time points)*

Test was attempted: ☐ No ☐ Yes

Time to walk 4 meters (trial 1) ____:____ (sec: two decimals)

Time to walk 4 meters (trial 2) ____:____ (sec: two decimals)

For data entry only- record faster time.

TKA/THA NERVE BLOCK STUDY

Form CEX

Clinical Exam Form

Version 06/03/2016

Study ID _____ PT Initials _____ Data Entry Initials _____ Form Date ____/____/____

FUNCTIONAL INDEPENDENCE MEASURE – FIM *(all form time points)*

Pain before FIM (0 - 10): _____

Transfers FIM

Test was attempted: ☐ No ☐ Yes

Score: _____

Supine to Sit: _____

Sit to Supine: _____

Sit to Stand: _____

Stand to Sit: _____

Bed Mobility: _____

FIM Transfers – Score coding:

1. Total assistance – contributes <25% of effort or unable to do
2. Maximal assistance – performs 25 – 50% of task
3. Moderate assistance – performs 50-75% of task
4. Minimal assistance – incidental hands-on help (> 75% of task)
5. Supervision – standby or verbal prompt or help with setup
6. Modified independence - Require device but no physical help
7. Fully independent

Gait FIM

Test was attempted: ☐ No ☐ Yes

Score: _____

Distance: _____ ft

Assistive Device: ☐ None

☐ Walker

☐ Cane

☐ Other: _____

Level of Assistance: _____

FIM Gait – Score coding:

1. Total assistance; <50 ft OR needs 2 helpers, <25% effort
2. Maximal assistance; 50 – 150 ft, 25 – 50% of task effort
3. Moderate assistance; 50-75% of task effort
4. Minimal assistance; > 75% of task effort, contact assistance (through corners & door cells), 150 ft.
5. Supervision; 150 ft, standby or verbal prompt
6. Modified independence; 150 ft, needs AD, more time, safety concerns
7. Fully independent; 150 ft, safe, reasonable time

Stairs FIM

Test was attempted: ☐ No ☐ Yes

Score: _____

Number of Steps: _____

Assistive Handrail Used: ☐ No ☐ Yes

Assistive Device: ☐ None

☐ Walker

☐ Cane

☐ Other: _____

Level of Assistance: _____

FIM Stairs – Score coding:

1. Total assistance; less than 4 steps OR needs 2 helpers, <25% effort
2. Maximal assistance; 4 to 11 steps, 25 – 50% of task effort
3. Moderate assistance; 12-14 steps, 50-75% of task effort
4. Minimal assistance; 12-14 steps, > 75% of task effort
5. Supervision; 12-14 steps, 100% effort, standby or prompt
EXCEPTION: 4-6 steps independently with or no AD
6. Modified independence; 12-14 steps, uses device, rails, orthoses
7. Fully independent; 12-14 steps, timely, safe, no rail

TKA/THA NERVE BLOCK STUDY			
Form CEX	Clinical Exam Form		Version 06/03/2016
Study ID _____	PT Initials _____	Data Entry Initials _____	Form Date ____/____/____

REPEATED CHAIR STAND TEST *(baseline, post-op 2, post-op 3, post-op 4, post-op 5, and week 6)*

Test was attempted: ☐ Yes ☐ No

Time to complete five stands: ____:____ ____ (sec: two decimals)

☐ Test was attempted but participant could not complete 5 stands (if this is checked, leave time to complete test blank).

Use the foam pad over the seat of the chair for patients post total hip arthroplasty so that hip flexion is not more than 90 degrees during testing.

STAIR CLIMBING TIME *(baseline, week 6)*

Test was attempted: ☐ No ☐ Yes

Time : ____:____ ____ (sec: two decimals)

SINGLE-LEG BALANCE TEST *(baseline, week 6)*

Test was attempted: ☐ No ☐ Yes

Side	Trial 1	Trial 2	Trial 3
____ Non-surgical side:	_____	_____	_____ (sec: two decimals)
____ Surgical side:	_____	_____	_____ (sec: two decimals)

☐ Pain after all tests – 0 to 10 *(all form time points)*: ____

Comments: _____

TKA/THA NERVE BLOCK STUDY			
Form CEX	Clinical Exam Form		Version 06/03/2016
Study ID _____	PT Initials _____	Data Entry Initials _____	Form Date ____/____/____

ADDITIONAL TREATMENT INFORMATION *(all post-op days)*

Therapeutic Exercise:

- | | |
|--|-------|
| ☐ Ankle Pumps | Reps: |
| ☐ Knee PROM | Reps: |
| ☐ Knee AROM | Reps: |
| ☐ Hip PROM | Reps: |
| ☐ Hip AROM | Reps: |
| ☐ Straight leg raises | Reps: |
| ☐ Quad sets | Reps: |
| ☐ Gluteal sets | Reps: |
| ☐ Hamstrings sets | Reps: |
| ☐ Heel slides | Reps: |
| ☐ Short arc quads | Reps: |
| ☐ Hip ABD/ADD | Reps: |
| ☐ Bridging | Reps: |
| ☐ Other | |
| ☐ Other | |

Comments: _____

Date of discharge *(discharge day only)*: ____/____/____

- ☐ CPRS source document printed

TKA/THA NERVE BLOCK STUDY

Form CONMEDS

Concurrent Medications

Final 01/15/2016

Study ID _____

Staff Initials _____

Form Date ____/____/____

Are you currently taking any medications (prescription, over the counter, vitamins, minerals, supplements), or non-drug therapy? ☐ Yes ☐ No

#	Medication/ Non-drug Therapy	Indication	Dose (per admin)	Dose Units ¹	Schedule/ Frequency ²	Dose Form ³	Route of Administration ⁴	Start Date	End Date	Baseline Med (Y/N)	Continuing at end of study (Y/N)

Dose Units¹

1 - g (gram)
 2 - mg (milligram)
 3 - µg (microgram)
 4 - L (liter)
 5 - mL (milliliter)
 6 - IU (International Unit)
 7 - Other

Schedule (frequency)²

1 - QD (once a day) 7 - QOM (every other mo)
 2 - BID (twice a day) 8 - QH (every hour)
 3 - TID (three times a day) 9 - AC (before meals)
 4 - QID (four times a day) 10 - PC (after meals)
 5 - QOD (every other day) 11 - PRN (as needed)
 6 - QM (every month) 12 - Once only
 13 - Other

Dose Form³

1 - Tablet 7 - Suspension
 2 - Capsule 8 - Patch
 3 - Ointment 9 - Gas
 4 - Suppository 10 - Gel
 5 - Aerosol 11 - Cream
 6 - Spray 12 - Powder

Route of Administration⁴

1 - Oral 8 - Inhalation
 2 - Topical 9 - Intravenous
 3 - Subcutaneous 10 - Intraperitoneal
 4 - Intradermal 11 - Nasal
 5 - Transdermal 12 - Vaginal
 6 - Intraocular 13 - Rectal
 7 - Intramuscular 14 - Other

TKA/THA NERVE BLOCK STUDY		
Form CONS	Consent Verification	Final 08/24/2016
Study ID _____	Staff Initials ____ _	Form Date ____/____/____

INSTRUCTIONS: Record all agreements determined before signing of consent

1. Agrees to be randomized ☐ Yes ☐ No
2. Understands that GA is not used except as backup plan ☐ Yes ☐ No
3. Agrees to survey completion before surgery, throughout hospital stay, and at return visit at two and six weeks ☐ Yes ☐ No
4. Agrees to PT/OT testing before surgery, throughout hospital stay, and at a return visit at six weeks ☐ Yes ☐ No
5. The study has been discussed with the subject and all questions were answered. ☐ Yes ☐ No
6. Date of Enrollment / signing of consent ____/____/____
7. The subject has been provided with a SIGNED and DATED copy of the Informed Consent Form. ☐ Yes ☐ No

TKA/THA NERVE BLOCK STUDY		
Form DCR	Discharge Disposition and Rehabilitation	Final 05/23/2016
Study ID _____	Staff Initials _____	Form Date ____/____/____

Visit: ☐ 6 Weeks

1. Date of hospital discharge: ____/____/____

2. After hospital discharge, where did you go?
(Check all that apply)

☐ Home

☐ Inpatient Rehabilitation Facility

☐ Skilled Nursing Facility

☐ Other, _____

2.1. For the settings other than Home, how many days were you at each applicable setting?

Inpatient Rehabilitation Facility _____ days

Skilled Nursing Facility _____ days

Other _____ days

2.2. If you were discharged to an Inpatient Rehabilitation Facility, Skilled Nursing Facility, or Other, what date did you arrive at home? ____/____/____

2.3. After hospital discharge, have you been re-admitted to a hospital? ☐ Yes ☐ No

3. Did you have rehabilitation for your [knee/hip] replacement after hospital discharge? ☐ Yes ☐ No

If Yes,

3.1 Where was it done?
(Check all that apply)

☐ Home

☐ Inpatient Rehabilitation Facility

☐ Skilled Nursing Facility

☐ Outpatient Facility

3.2 Number of days _____ days

3.3 Sessions per day _____ sessions / day (on average)

3.4 Duration of each session _____ minutes (on average)

TKA/THA NERVE BLOCK STUDY		
Form DCR	Discharge Disposition and Rehabilitation	Final 05/23/2016
Study ID _____	Staff Initials _____	Form Date ____/____/____

3.5 Content of rehabilitation

- ☐ Pain/swelling control
- ☐ Knee/hip range of motion
- ☐ Gait training
- ☐ Aerobic training
- ☐ High intensity strengthening
- ☐ Low intensity strengthening
- ☐ Functional training

3.6 On a scale of 0 (no effort) to 100 (the effort that you put into basic training in military service), how much effort did you put into physical therapy after hospital discharge?

No effort (0)	_____	As much as in basic training (100)
---------------------	-------	--

TKA/THA NERVE BLOCK STUDY

Form DEM

Demographics

Final 04/06/2016

Study ID _____

Staff Initials ____

Form Date ____ / ____ / ____

1. Date of birth ____ / ____ / ____
mm dd yyyy

2. Age ____ years

3. Are you Hispanic or Latino? ☐ Yes ☐ No

4. With which race(s) do you identify? (check all that apply)

☐ American Indian or Alaskan Native

☐ Asian

☐ Black or African American

☐ Native Hawaiian or other Pacific Islander

☐ White

☐ Other, specify _____

I would like to learn more about you, especially your background, activities and health.

5. Do you live alone? ☐ Yes ☐ No

If No:

5.1 Who lives with you? (check all that apply)

☐ Spouse

☐ Child

☐ Friend

☐ Other Relative

☐ Paid Employee

☐ Other, specify _____

☐ Refused

5.2 Including yourself, how many live in your household?

☐ Refused

6. Which of the following best describes your current marital status? (select only one)

☐ Married, or cohabiting

☐ Separated

☐ Divorced

☐ Widowed

☐ Never married

☐ Other, specify _____

☐ Refused

7. What was the highest grade or level of education you completed? (select only one)

☐ No formal education

☐ Elementary school (K-8)

☐ High school / GRE / equivalent (9-12)

☐ College

☐ Post graduate

☐ Other, specify _____

☐ Refused

TKA/THA NERVE BLOCK STUDY		
Form DEM	Demographics	Final 04/06/2016
Study ID _____	Staff Initials ____	Form Date ____ / ____ / ____

Demographics

Final 04/06/2016

Study ID _____

Staff Initials _____

Form Date ____ / ____ / ____

- Page 2 of 2

TKA/THA NERVE BLOCK STUDY		
Form DDAY	Discharge Day	Final 06/17/2016
Study ID _____	Staff Initials _____	Form Date ____/____/____

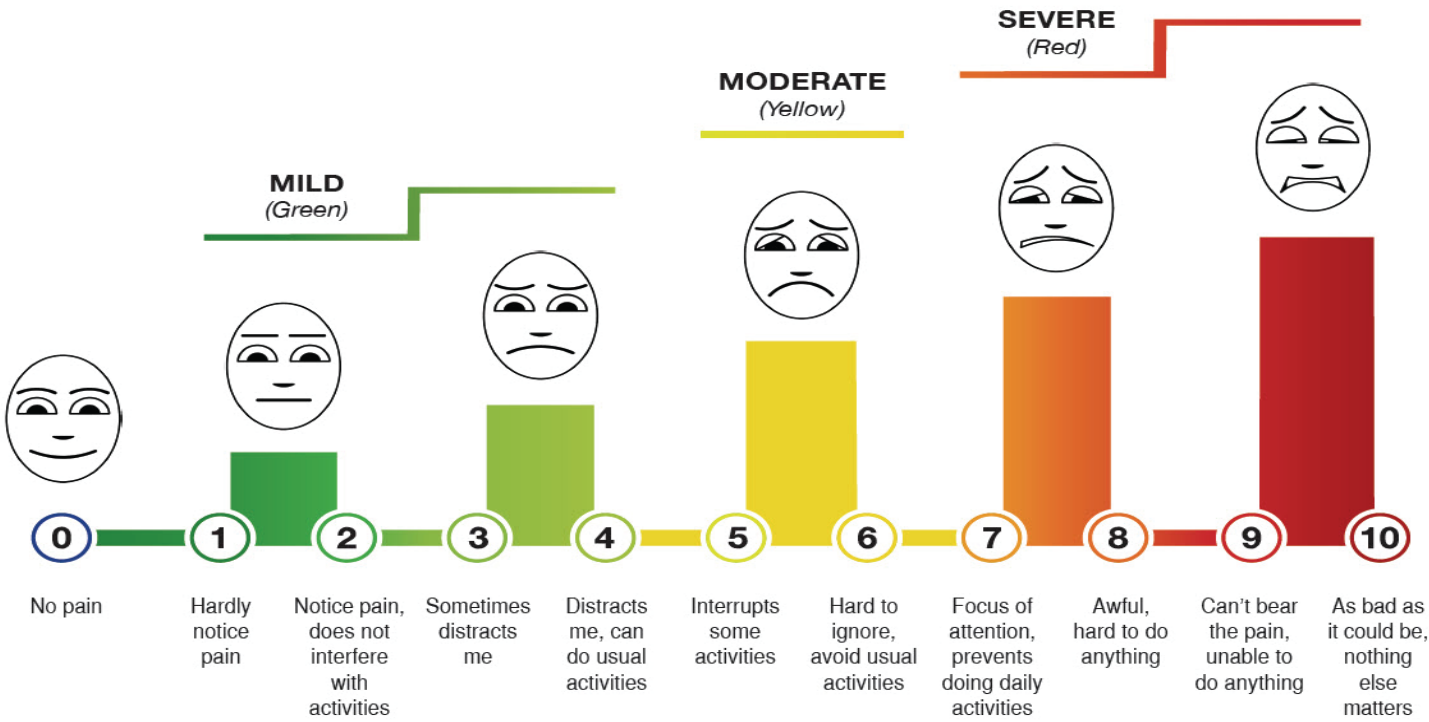
Day of Discharge: _____

Time of Discharge: _____

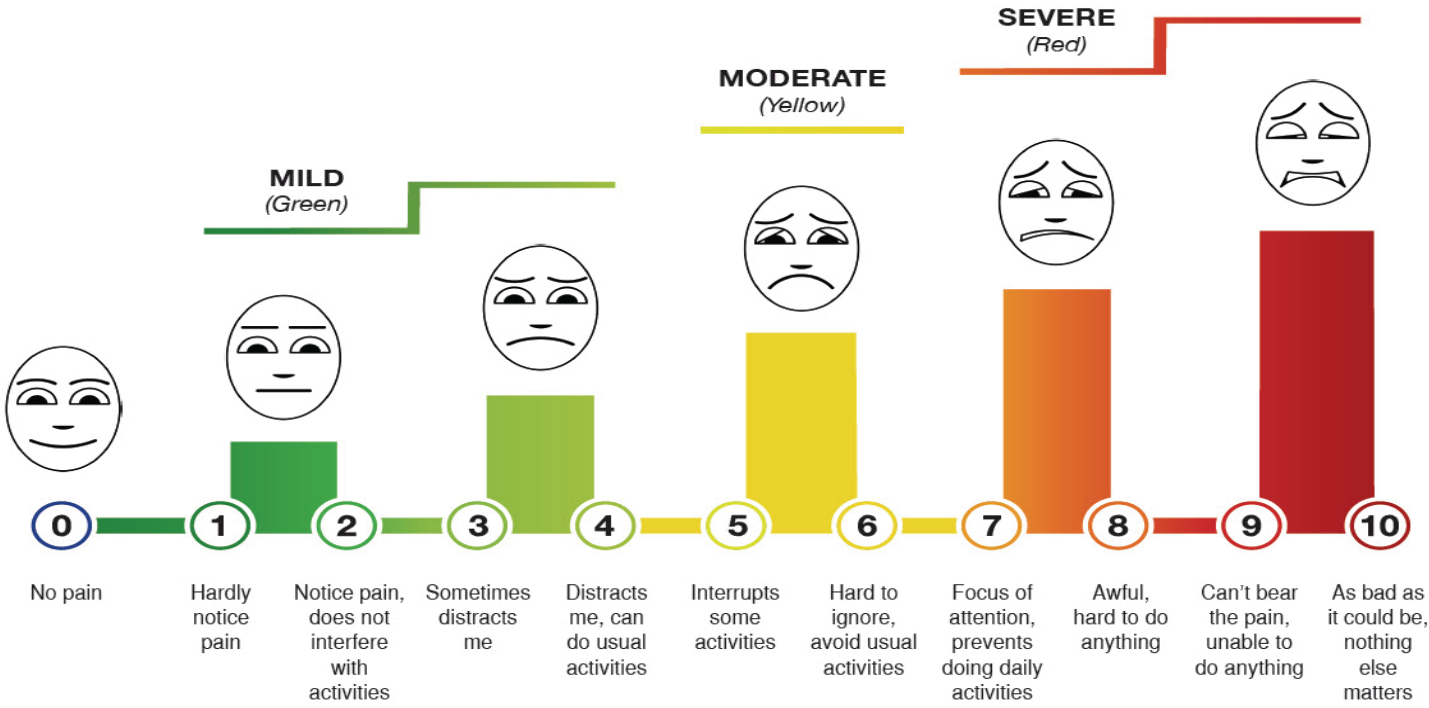
TKA/THA NERVE BLOCK STUDY		
Form DVPRS	Defense and Veterans Pain Rating Scale	Final 04/12/2016
Study ID _____	Staff Initials ____	Form Date / /

Visit: ☐ Baseline ☐ DOS Pre-Procedure ☐ DOS Post-Procedure ☐ Week 2 ☐ Week 6 Time: _____

1. Please rate the level of pain on **your SURGICAL [KNEE/HIP], AT REST**, in the last 24 hr.



2. Please rate the **WORST** level of pain on **your SURGICAL [KNEE/HIP], WITH MOVEMENT**, in the last 24 hr.



3. Please rate the impact of pain from your surgical [knee/hip] in the last 24 hr.

1. Circle the one number that describes how, during the past 24 hours, pain has interfered with your usual ACTIVITY:

0 1 2 3 4 5 6 7 8 9 10
Does not interfere Completely interferes

2. Circle the one number that describes how, during the past 24 hours, pain has interfered with your SLEEP:

0 1 2 3 4 5 6 7 8 9 10
Does not interfere Completely interferes

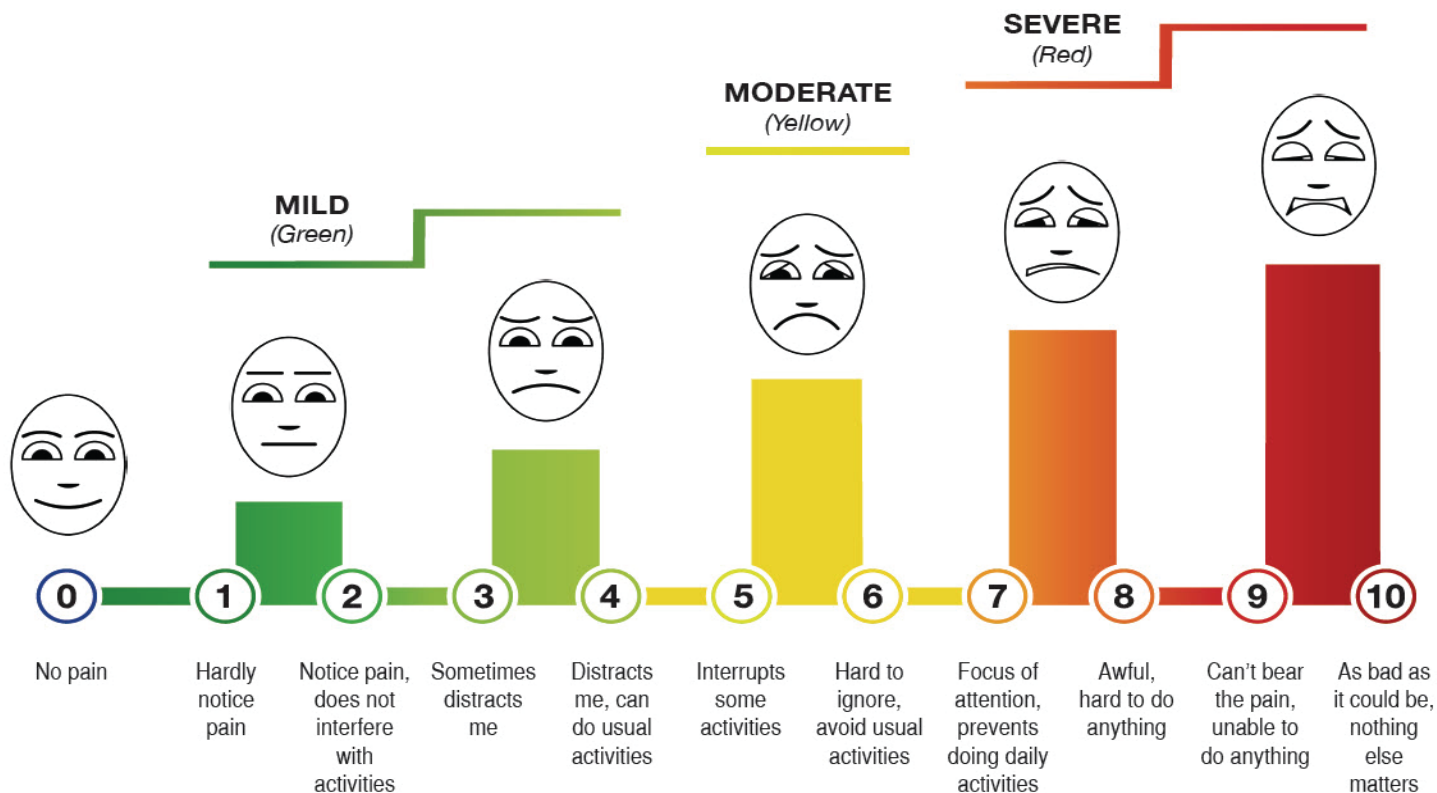
3. Circle the one number that describes how, during the past 24 hours, pain has affected your MOOD:

0 1 2 3 4 5 6 7 8 9 10
Does not affect Completely affects

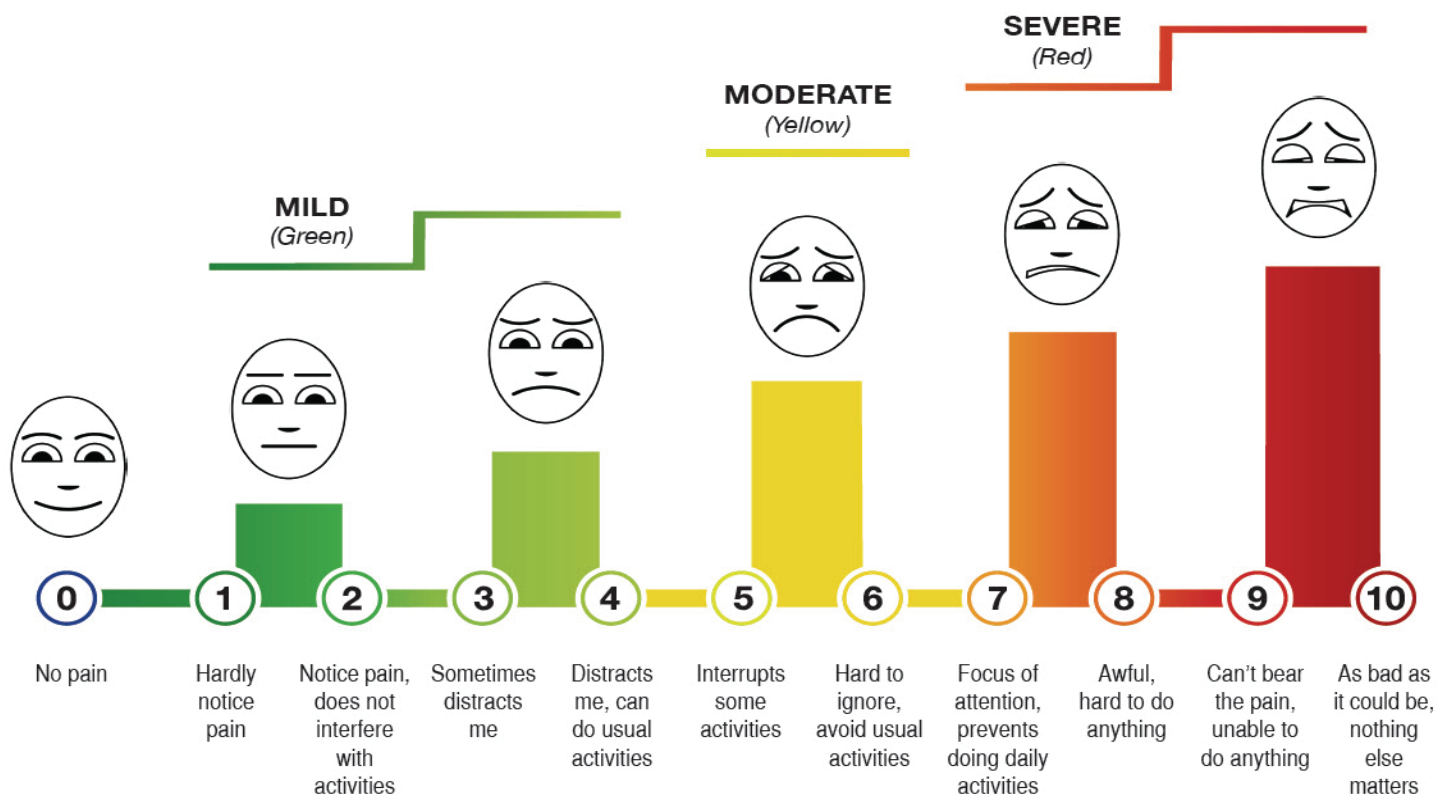
4. Circle the one number that describes how, during the past 24 hours, pain has contributed to your STRESS:

0 1 2 3 4 5 6 7 8 9 10
Does not contribute Contributes a great deal

4. Please rate the level of pain on **your OTHER [KNEE/HIP], AT REST**, in the last 24 hr.



5. Please rate the **WORST** level of pain on **your OTHER [KNEE/HIP], WITH MOVEMENT**, in the last 24 hr.



TKA/THA NERVE BLOCK STUDY

Form DVPRSIH

Defense and Veterans Pain Rating Scale

Final 05/03/2016

Study ID _____

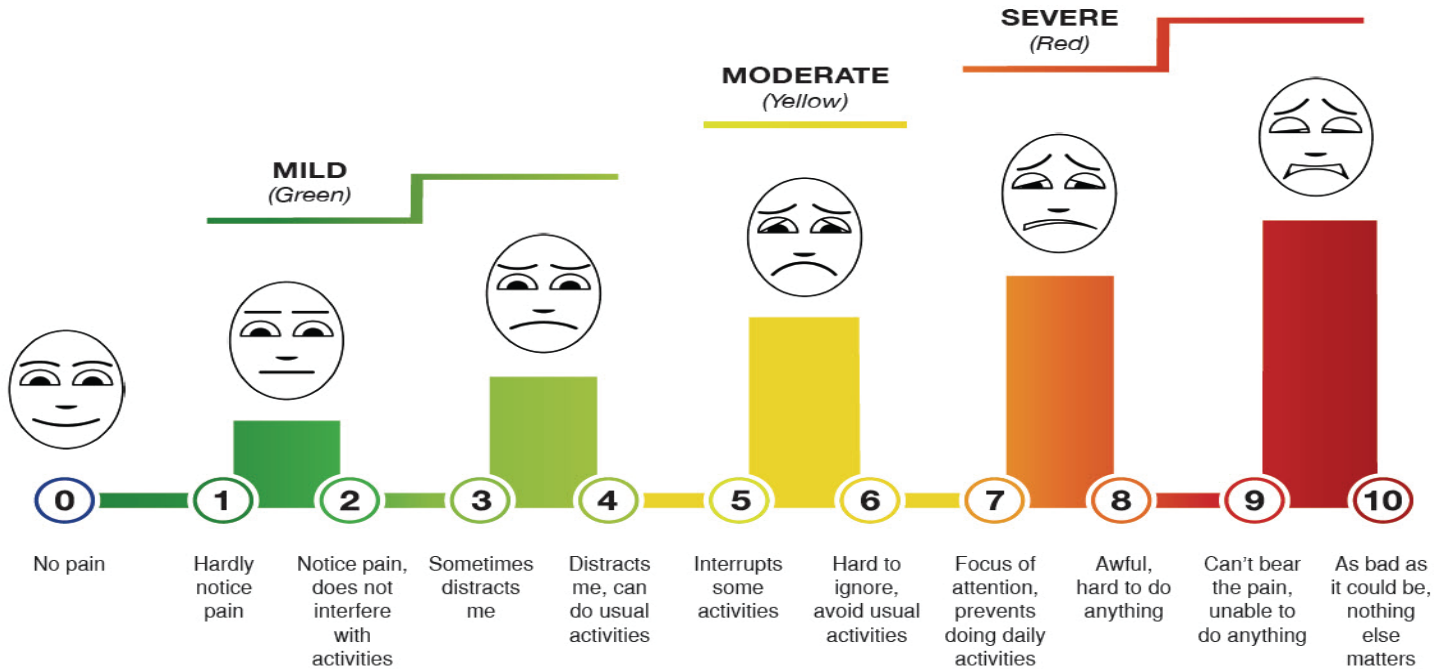
Staff Initials _____

Form Date ____/____/____

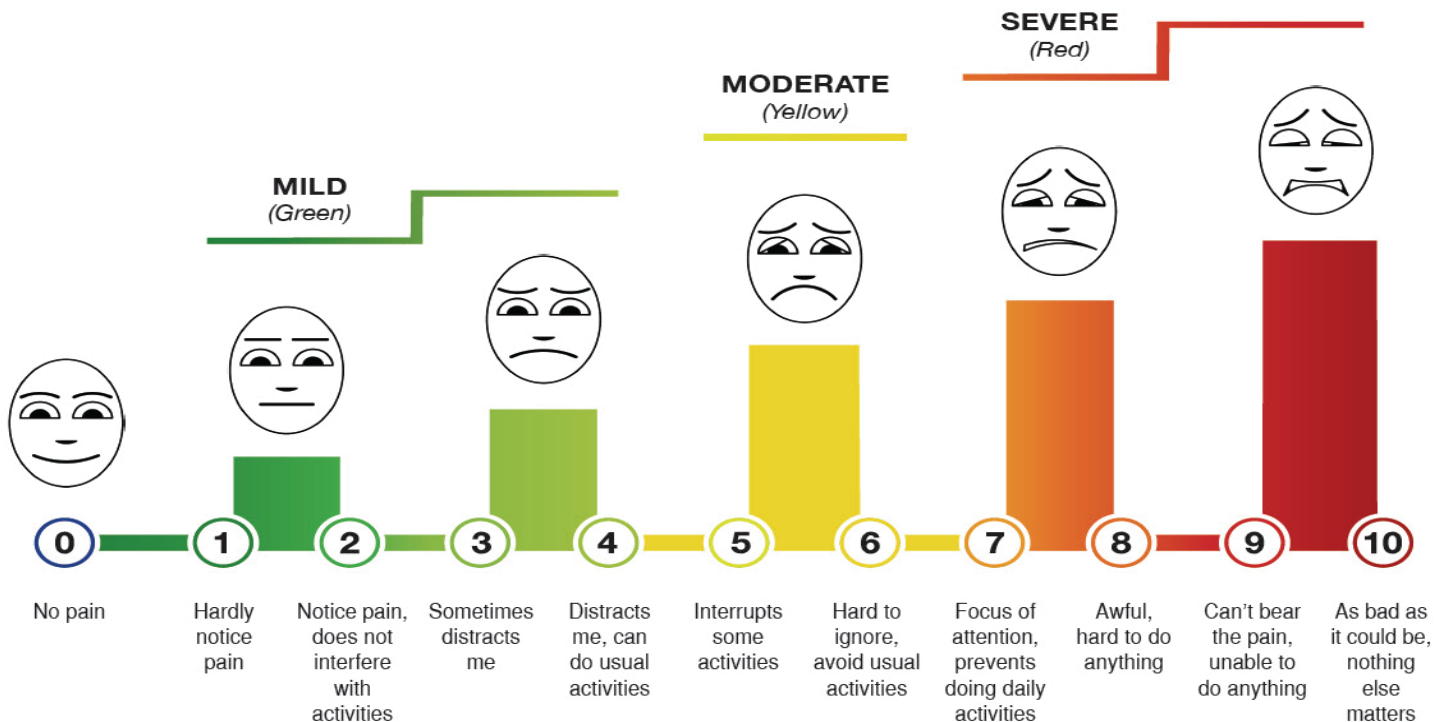
Visit: ☐ Post-Op 1 ☐ Post-Op 2 ☐ Post-Op 3 ☐ Post-Op 4 ☐ Post-Op 5

Time: _____

1. Please rate the level of pain on your **SURGICAL [KNEE/HIP], AT REST**, in the last 24 hr.



2. Please rate the **WORST** level of pain on your surgical [knee/hip], **WITH MOVEMENT**, in the last 24 hr.



2a. What time of day in the past 24 hours did you have your worst SURGICAL KNEE/HIP pain? (date-time)

____ : ____

“KWIKN” evaluation:

3. Date/Time knee/hip **STARTED** having pain: _____ / _____ (n/a)
4. Date/Time when nerve block numbness entirely wore off _____ / _____ (unsure)
- Before surgery, you said your worst pain score (at the time) with movement was _____ /10.
5. Knowing **What you Know Now**, compare your worst pain in the past 24 hours to your pain with movement before surgery:
- ☐ Less “now” ☐ Equal “now” ☐ More “now”
- 5a. What number would you give your before-surgery worst pain with movement, _____ (0-10)
Knowing **What you Know Now**?
6. Date/Time nerve block stopped providing pain relief _____ / _____ (unsure)
7. Date/Time when I first needed to take **oral opioid** pain medication, and it helped _____ / _____ (n/a)
8. Date/Time when I first needed **oral opioid** pain medication, but it did not help _____ / _____ (n/a)
9. Date/Time when I first needed **IV opioid** pain medication, and it helped _____ / _____ (n/a)
10. Date/Time when I first needed **IV opioid** pain medication, but it did not help _____ / _____ (n/a)

DEFENSE AND VETERANS PAIN RATING SCALE - SUPPLEMENTAL Qs FOR BIOPSYCHOSOCIAL IMPACT

11. Please rate the impact of pain from your **surgical [knee/hip]** in the last 24 hr.

1. Circle the one number that describes how, during the past 24 hours, pain has interfered with your usual **ACTIVITY**:

0 1 2 3 4 5 6 7 8 9 10
Does not interfere Completely interferes

2. Circle the one number that describes how, during the past 24 hours, pain has interfered with your **SLEEP**:

0 1 2 3 4 5 6 7 8 9 10
Does not interfere Completely interferes

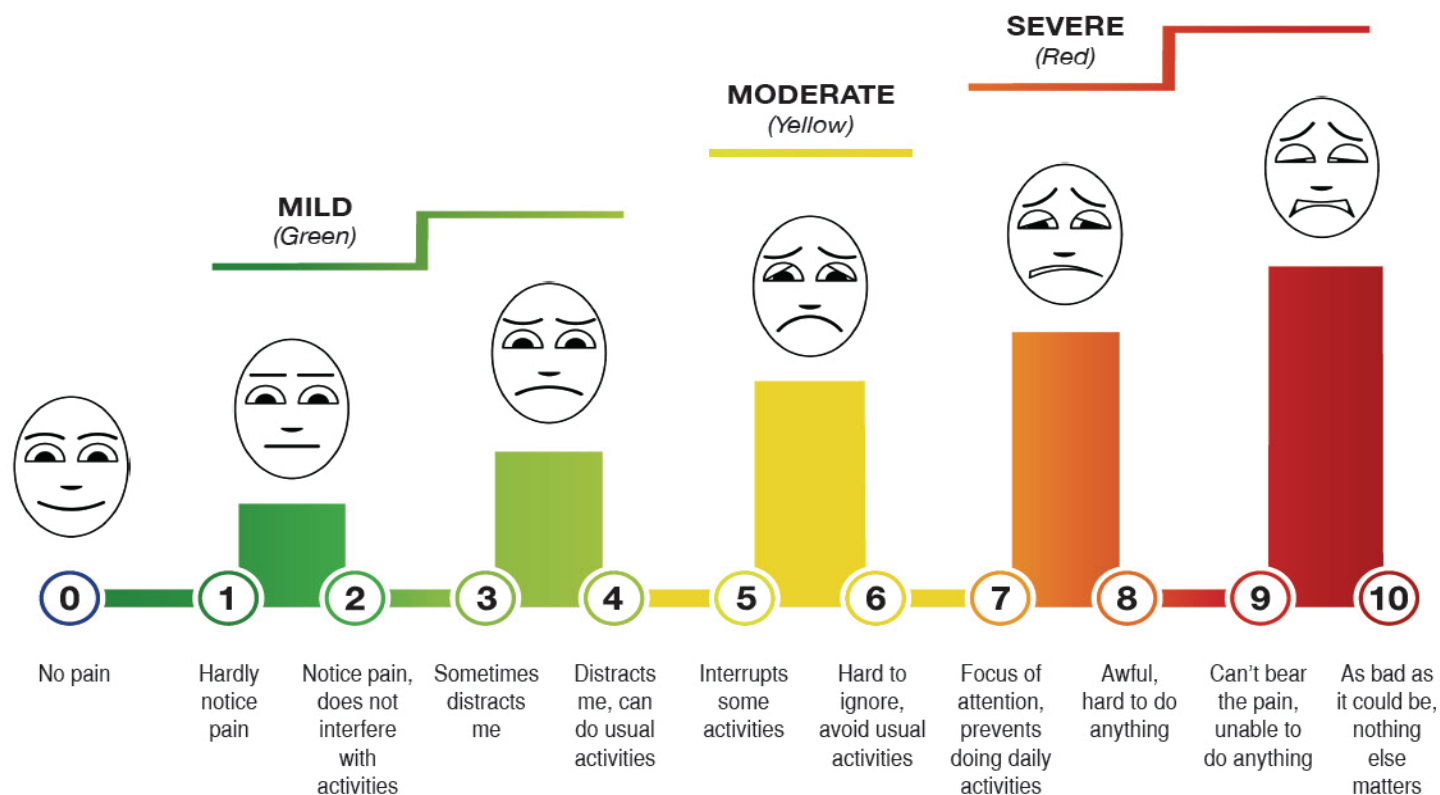
3. Circle the one number that describes how, during the past 24 hours, pain has affected your **MOOD**:

0 1 2 3 4 5 6 7 8 9 10
Does not affect Completely affects

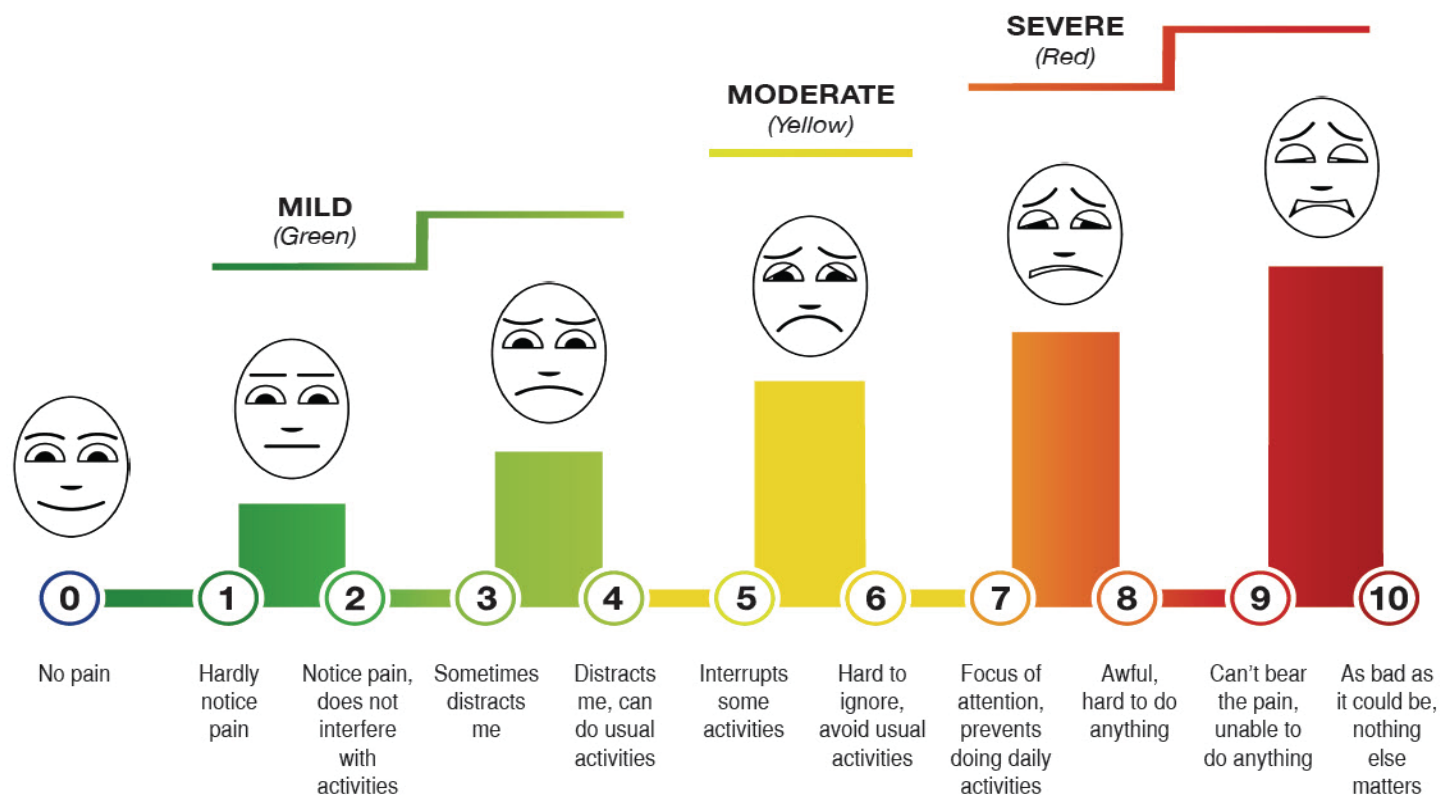
4. Circle the one number that describes how, during the past 24 hours, pain has contributed to your **STRESS**:

0 1 2 3 4 5 6 7 8 9 10
Does not contribute Contributes a great deal

12. Please rate the level of pain on **your OTHER [KNEE/HIP], AT REST**, in the last 24 hr.



13. Please rate the **WORST** level of pain on **your OTHER [KNEE/HIP], WITH MOVEMENT**, in the last 24 hr.



For coordinator entry only for this day's assessment:

Worst pain score with movement (0-10): _____

Is this score the "peak-to-date"?

No **Yes**

TKA/THA NERVE BLOCK STUDY

Form ET

Early Termination

Final 06/06/2016

Study ID _____

Staff Initials ____

Form Date ____ / ____ / ____

THIS FORM IS TO BE COMPLETED ONLY WHEN PROTOCOL VISITS ARE TO BE STOPPED

1. Primary reason for early termination (select best choice):

☐ Moved from the area

☒ Lost to follow up: (missed several visits without contact, and unable to locate)

1.1 Date of last contact: ____ / ____ / ____ (mm/dd/yyyy)

1.2 Contact method: ☐ by phone ☐ in person

☐ Patient choice (comment below)

☐ Clinician choice (comment below)

☐ Other reason (comment below)

2. Last protocol visit completed:

☐ Screening

☐ Baseline

☐ Surgery

☐ Post-Op Day 1 ☐ Post-Op Day 2 ☐ Post-Op Day 3 ☐ Post-Op Day 4 ☐ Post-Op Day 5

☐ Week 2

Visit date: ____ / ____ / ____ (mm/dd/yyyy)

3. Does patient agree to complete the Week 6 follow-up visit? ☐ Yes ☐ No ☐ NA

3.1 If Yes, date scheduled: ____ / ____ / ____ (mm/dd/yyyy)

4. Comments:

☐ CPRS research note generated and printed

TKA/THA NERVE BLOCK STUDY		
Form EL	Eligibility	Final 04/06/2016
Study ID _____	Staff Initials _____	Form Date ____/____/____

Inclusion Criteria

1. Age between 18 and 85, and undergoing a total knee or hip replacement.	☐ Yes	☐ No
2. Fluent in English, decision competent, willing and able to provide written informed consent, and able to complete the study's schedule of assessments.	☐ Yes	☐ No
3. Able to walk >3m without an assisting device.	☐ Yes	☐ No
4. Have a BMI ≤ 40 kg/m ² .	☐ Yes	☐ No
If any No, disqualify		

Exclusion Criteria

1. Current participation in another orthopedic/PT/rehab/anesthesiology interventional clinical trial.	☐ Yes	☐ No
2. Are at significant behavioral risks or have refractory major psychiatric disorders.	☐ Yes	☐ No
3. Revision surgery on the same extremity.	☐ Yes	☐ No
4. Have an ASA Physical Status classification of 4 or higher.	☐ Yes	☐ No
5. Have been diagnosed with clinically significant neuropathy with its origins in either diabetes or other causes; have neuromuscular disease that would influence data collection.	☐ Yes	☐ No
6. Have a surgically-fused lumbar spine, or a spinal cord simulator, or other condition that would contraindicate or prohibit the conduct of spinal anesthesia.	☐ Yes	☐ No
7. At significant risk for postoperative substance abuse, or immediate-postoperative substance abuse withdrawal symptoms (alcohol, cocaine, enrolled in methadone or buprenorphine opioid withdrawal programs, etc.).	☐ Yes	☐ No
8. Are undergoing TKA/THA for a tumor.	☐ Yes	☐ No
9. Have contraindications (e.g., anaphylaxis) to any of the study drugs.	☐ Yes	☐ No
10. Have a systemic fungal infection.	☐ Yes	☐ No
11. Have a known hypersensitivity to bupivacaine hydrochloride or to any local anesthetic of the amide-type or to other components of bupivacaine hydrochloride solutions.	☐ Yes	☐ No
12. Have a known or suspected buprenorphine hypersensitivity (not including nausea and/or vomiting).	☐ Yes	☐ No
13. Have a GI obstruction.	☐ Yes	☐ No

TKA/THA NERVE BLOCK STUDY		
Form EL	Eligibility	Final 04/06/2016
Study ID _____	Staff Initials _____	Form Date ____/____/____

14. Have paralytic ileus.

15. If female, pregnancy

☐ Yes	☐ No	☐ NA
☐ Yes	☐ No	
If any Yes, disqualify		

Eligibility determination: ☐ Eligible ☐ Not eligible (disqualified)

Source documents verified and printed from CPRS:

- ☐ IMPACT RN note
- ☐ IMPACT NP/MD note
- ☐ Associated addenda

I verify this individual is eligible for inclusion in this study.

_____	_____
PI Signature	Date

TKA/THA NERVE BLOCK STUDY		
Form FALLS-IH	Falls History – Short Form	Final 05/03/2016
Study ID _____	Staff Initials _____	Form Date ____/____/____

Visit: ☐ Post-Op 1 ☐ Post-Op 2 ☐ Post-Op 3 ☐ Post-Op 4 ☐ Post-Op 5

1. Have you had a fall **today**?

☐ Yes ☐ No

If Yes,

1.1 Have you fallen more than once today? ☐ Yes ☐ No If Yes, <table border="1"> <tr> <td>1.1.1 How many times have you fallen today?</td> <td> ☐ 2 times ☐ 3 times ☐ 4 times ☐ 5 times ☐ between 6 and 10 times ☐ more than 10 times </td> </tr> </table> 1.2 Did you seek medical treatment after any of your falls? ☐ Yes ☐ No 1.3 Did you need help to get up after any of the falls? ☐ Yes ☐ No	1.1.1 How many times have you fallen today ?	☐ 2 times ☐ 3 times ☐ 4 times ☐ 5 times ☐ between 6 and 10 times ☐ more than 10 times
1.1.1 How many times have you fallen today ?	☐ 2 times ☐ 3 times ☐ 4 times ☐ 5 times ☐ between 6 and 10 times ☐ more than 10 times	

2. Today, have you lost your balance or started to fall but caught yourself?

☐ Yes ☐ No

If Yes,

2.1 How often do you lose your balance?	☐ rarely/almost never ☐ sometimes/ every now and then ☐ regularly
---	--

3. Are you afraid of falling?

☐ Yes ☐ No

☐ Source document verified and printed from CPRS

TKA/THA NERVE BLOCK STUDY

Form FALLS-Post

Falls History – Short Form

Final 02/12/2016

Study ID _____

Staff Initials _____

Form Date ____/____/____

Visit: ☐ Week 6

1. Have you had a fall ***after hospital discharge***?

☐ Yes ☐ No

If Yes,

1.1 Have you fallen more than once ***after hospital discharge***?

☐ Yes ☐ No

If Yes,

1.1.1 How many times have you fallen
after hospital discharge?

- ☐ 2 times
- ☐ 3 times
- ☐ 4 times
- ☐ 5 times
- ☐ between 6 and 10 times
- ☐ more than 10 times

1.2 Did you seek medical treatment after any of your falls?

☐ Yes ☐ No

1.3 Were you hospitalized after any of your falls?

☐ Yes ☐ No

1.4 Did you need help to get up after any of the falls?

☐ Yes ☐ No

2. After hospital discharge, have you lost your balance or started to fall but caught yourself?

☐ Yes ☐ No

If Yes,

2.1 How often do you lose your balance?

- ☐ rarely/almost never
- ☐ sometimes/ every now and then
- ☐ regularly

3. Are you afraid of falling?

☐ Yes ☐ No

☐ Source document verified and printed from CPRS

TKA/THA NERVE BLOCK STUDY

Form FALLS-Pre

Falls History – Short Form

Final 01/15/2016

Study ID _____

Staff Initials ____

Form Date ____ / ____ / ____

Visit: ☐ Baseline

1. Have you had a fall *in the past year*?

☐ Yes ☐ No

If Yes,

1.1 Have you fallen more than once
in the past year?

☐ Yes ☐ No

If Yes,

1.1.1 How many times have you fallen
in the past year ?

- ☐ 2 times
- ☐ 3 times
- ☐ 4 times
- ☐ 5 times
- ☐ between 6 and 10 times
- ☐ more than 10 times

1.2 Did you seek medical treatment after any of your falls?

☐ Yes ☐ No

1.3 Were you hospitalized after any of your falls?

☐ Yes ☐ No

1.4 Did you need help to get up after any of the falls?

☐ Yes ☐ No

2. In the past year, have you ever lost your balance or started to fall but caught yourself?

☐ Yes ☐ No

If yes,

2.1 How often do you lose your balance?

- ☐ rarely/almost never
- ☐ sometimes/ every now and then
- ☐ regularly

3. Are you afraid of falling?

☐ Yes ☐ No

TKA/THA NERVE BLOCK STUDY

Form ICHG	Interim Changes in Signs & Symptoms, Illness, and Additional Treatment Seeking	Final 02/12/2016
Study ID _____	Staff Initials ____	Form Date ____ / ____ / ____

Visit: ☐ Week 6

Please answer the following questions about changes since our last physical therapy contact:

1. Regarding your replaced **[knee/hip]**, indicate any change in:

- 1.1 Pain ☐ Improved ☐ Worsened ☐ No change since last evaluation
- 1.2 Swelling ☐ Improved ☐ Worsened ☐ No change since last evaluation
- 1.3 Stiffness ☐ Improved ☐ Worsened ☐ No change since last evaluation

2. Have you been limping while walking because of your **[knee/hip]** surgery? ☐ Yes ☐ No
If Yes,

2.1 Is it a new occurrence? ☐ Yes ☐ No

3. Has it been difficult for you to bear weight on the surgical **[knee/hip]**? ☐ Yes ☐ No
If Yes,

3.1 Is it a new occurrence? ☐ Yes ☐ No

4. Is your **[knee/hip]** pain preventing you from performing activities? ☐ Yes ☐ No
If Yes,

4.1 Is it a new occurrence? ☐ Yes ☐ No

4.2 What activity? _____

The remaining questions are to be completed at the Week 6 evaluation only.

5. Did you seek a health care professional regarding your **[knee/hip]** pain? ☐ Yes ☐ No
If Yes,

5.1 Please describe: _____

6. Have you been hospitalized or disabled (> ½ day in bed, or required to cut back on routine activities)? ☐ Yes ☐ No
If Yes,

6.1 Reason: _____

6.2 For how long? ____ days

7. Have you participated in any rehabilitation or exercise interventions? ☐ Yes ☐ No
If Yes,

7.1 What activity (content)? _____

7.2 How often? ____ times per week

7.3 Duration of activity? ____ minutes

TKA/THA NERVE BLOCK STUDY

Form OPIOID

**Opioid Consumption
(in hospital, log from CPRS BCMA)**

Final 01/15/2016

Study ID _____

Staff Initials ____

Form Date ____/____/____

Day of Surgery ____/____/____

PACU Discharge Time (military) ____:____

0-24 hr after PACU Discharge: Start Date: ____/____/____ Start Time (military) ____:____
End Date: ____/____/____ End Time (military) ____:____

24-48 hr after PACU Discharge: Start Date: ____/____/____ Start Time (military) ____:____
End Date: ____/____/____ End Time (military) ____:____

48-72 hr after PACU Discharge: Start Date: ____/____/____ Start Time (military) ____:____
End Date: ____/____/____ End Time (military) ____:____

72-96 hr after PACU Discharge: Start Date: ____/____/____ Start Time (military) ____:____
End Date: ____/____/____ End Time (military) ____:____

>96 hr after PACU Discharge: Start Date: ____/____/____ Start Time (military) ____:____
End Date: ____/____/____ End Time (military) ____:____

Total opioids:

<i>Opioid name and route</i>	<i>MG for 0-24hr</i>	<i>MG for 24.1 - 48hr</i>	<i>MG 48.1 - 72hr</i>	<i>MG 72.1 - 96 hr</i>	<i>MG > 96hr</i>
Oxycodone po					
SR morphine po					
Hydromorphone IV					
Morphine IV					

Other (drug name and total):

☐ CPRS source document verified and printed.

TKA/THA NERVE BLOCK STUDY

Form QOR15	Quality of Recovery	Final 05/03/2016
Study ID _____	Staff Initials ____	Form Date ____ / ____ / ____

Visit: ☐ Baseline ☐ Post-Op Day 1 ☐ Post-Op Day 2 ☐ Post-Op Day 3 ☐ Post-Op Day 4 ☐ Post-Op Day 5

☐ Week 6 Time: _____

PART A:

How have you been feeling in the last 24 hours?

(0 to 10, where 0 = none of the time [poor] and 10 = all of the time [excellent])

- | | | | |
|---|------------------|---|-----------------|
| 1. Able to breathe easily | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 0 1 2 3 4 5 6 7 8 9 10 </div> | All of the time |
| 2. Been able to enjoy food | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 0 1 2 3 4 5 6 7 8 9 10 </div> | All of the time |
| 3. Feeling rested | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 0 1 2 3 4 5 6 7 8 9 10 </div> | All of the time |
| 4. Have had a good sleep | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 0 1 2 3 4 5 6 7 8 9 10 </div> | All of the time |
| 5. Able to look after personal toilet and hygiene unaided | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 0 1 2 3 4 5 6 7 8 9 10 </div> | All of the time |
| 6. Able to communicate with family or friends | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 0 1 2 3 4 5 6 7 8 9 10 </div> | All of the time |
| 7. Getting support from hospital doctors and nurses | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 0 1 2 3 4 5 6 7 8 9 10 </div> | All of the time |
| 8. Able to return to work or usual home activities | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 0 1 2 3 4 5 6 7 8 9 10 </div> | All of the time |
| 9. Feeling comfortable and in control | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 0 1 2 3 4 5 6 7 8 9 10 </div> | All of the time |
| 10. Having a feeling of general well-being | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 0 1 2 3 4 5 6 7 8 9 10 </div> | All of the time |

PART B:

Have you had any of the following in the last 24 hours?

(10 to 0, where 10 = none of the time [excellent] and 0 = all of the time [poor])

- | | | | |
|--------------------------------|------------------|---|-----------------|
| 11. Moderate pain | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 10 9 8 7 6 5 4 3 2 1 0 </div> | All of the time |
| 12. Severe pain | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 10 9 8 7 6 5 4 3 2 1 0 </div> | All of the time |
| 13. Nausea or vomiting | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 10 9 8 7 6 5 4 3 2 1 0 </div> | All of the time |
| 14. Feeling worried or anxious | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 10 9 8 7 6 5 4 3 2 1 0 </div> | All of the time |
| 15. Feeling sad or depressed | None of the time | <div style="border-bottom: 1px solid black; position: relative; height: 1.2em;"> 10 9 8 7 6 5 4 3 2 1 0 </div> | All of the time |

Your Health and Well-Being

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. *Thank you for completing this survey!*

For each of the following questions, please mark an ☒ in the one box that best describes your answer.

- 1. Overall, how would you rate your health during the past 24 hours?**

Excellent	Very good	Good	Fair	Poor	Very Poor
▼	▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

- 2. During the past 24 hours, how much did physical health problems limit your usual physical activities (such as walking or climbing stairs)?**

Not at all	Very little	Somewhat	Quite a lot	Could not do physical activities
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

- 3. During the past 24 hours, how much difficulty did you have doing your daily work, both at home and away from home, because of your physical health?**

None at all	A little bit	Some	Quite a lot	Could not do daily work
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

4. How much bodily pain have you had during the past 24 hours?

None	Very mild	Mild	Moderate	Severe	Very Severe
▼	▼	▼	▼	▼	▼
☐ ₁	☐ ₂	☐ ₃	☐ ₄	☐ ₅	☐ ₆

5. During the past 24 hours, how much energy did you have?

Very much	Quite a lot	Some	A little	None
▼	▼	▼	▼	▼
☐ ₁	☐ ₂	☐ ₃	☐ ₄	☐ ₅

6. During the past 24 hours, how much did your physical health or emotional problems limit your usual social activities with family or friends?

Not at all	Very little	Somewhat	Quite a lot	Could not do social activities
▼	▼	▼	▼	▼
☐ ₁	☐ ₂	☐ ₃	☐ ₄	☐ ₅

7. During the past 24 hours, how much have you been bothered by emotional problems (such as feeling anxious, depressed or irritable)?

Not at all	Slightly	Moderately	Quite a lot	Extremely
▼	▼	▼	▼	▼
☐ ₁	☐ ₂	☐ ₃	☐ ₄	☐ ₅

8. During the past 24 hours, how much did personal or emotional problems keep you from doing your usual work, school or other daily activities?

Not at all	Very little	Somewhat	Quite a lot	Could not do daily activities
▼	▼	▼	▼	▼
☐ ₁	☐ ₂	☐ ₃	☐ ₄	☐ ₅

Thank you for completing these questions!

Your Health and Well-Being

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Thank you for completing this survey!

For each of the following questions, please mark an ☒ in the one box that best describes your answer.

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. Compared to one year ago, how would you rate your health in general now?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot ▼	Yes, limited a little ▼	No, not limited at all ▼
a <u>Vigorous activities</u> , such as running, lifting heavy objects, participating in strenuous sports	☐ 1	☐ 2	☐ 3
b <u>Moderate activities</u> , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
c Lifting or carrying groceries.....	☐ 1	☐ 2	☐ 3
d Climbing <u>several</u> flights of stairs.....	☐ 1	☐ 2	☐ 3
e Climbing <u>one</u> flight of stairs	☐ 1	☐ 2	☐ 3
f Bending, kneeling, or stooping	☐ 1	☐ 2	☐ 3
g Walking <u>more than a mile</u>	☐ 1	☐ 2	☐ 3
h Walking <u>several hundred yards</u>	☐ 1	☐ 2	☐ 3
i Walking <u>one hundred yards</u>	☐ 1	☐ 2	☐ 3
j Bathing or dressing yourself	☐ 1	☐ 2	☐ 3

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the <u>amount of time</u> you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b <u>Accomplished less</u> than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Were limited in the <u>kind of</u> work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d Had <u>difficulty</u> performing the work or other activities (for example, it took extra effort)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the <u>amount of time</u> you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b <u>Accomplished less</u> than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Did work or other activities <u>less carefully than usual</u>	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

7. How much bodily pain have you had during the past 4 weeks?

None	Very mild	Mild	Moderate	Severe	Very severe
▼	▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
	▼	▼	▼	▼	▼
a Did you feel full of life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Have you been very nervous?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Have you felt so down in the dumps that nothing could cheer you up?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f Have you felt downhearted and depressed?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g Did you feel worn out?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h Have you been happy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
i Did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
▼	▼	▼	▼	▼
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

11. How TRUE or FALSE is each of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
	▼	▼	▼	▼	▼
a I seem to get sick a little easier than other people	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b I am as healthy as anybody I know	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c I expect my health to get worse.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d My health is excellent.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Thank you for completing these questions!

TKA/THA NERVE BLOCK STUDY

Form SFMPQ2	Short-Form McGill Pain Questionnaire 2	Final 05/03/2016
Study ID _____	Staff Initials _____	Form Date ____/____/____

Visit: ☐ Baseline ☐ DOS Pre-procedure ☐ DOS Post-procedure ☐ Post-Op 1 ☐ Post-Op 2 ☐ Post-Op 3 ☐ Post-Op 4
☐ Post-Op 5 ☐ Week 6 Administration time: _____

This questionnaire provides you with a list of words that describe some of the different qualities of pain and related symptoms. Please put an **X** through the numbers that best describe the intensity of each of the pain and related symptoms you felt during the past week. Use 0 if the word does not describe your pain or related symptoms.

	None											Worst Possible
1. Throbbing pain	0	1	2	3	4	5	6	7	8	9	10	
2. Shooting pain	0	1	2	3	4	5	6	7	8	9	10	
3. Stabbing pain	0	1	2	3	4	5	6	7	8	9	10	
4. Sharp pain	0	1	2	3	4	5	6	7	8	9	10	
5. Cramping pain	0	1	2	3	4	5	6	7	8	9	10	
6. Gnawing pain	0	1	2	3	4	5	6	7	8	9	10	
7. Hot-burning pain	0	1	2	3	4	5	6	7	8	9	10	
8. Aching pain	0	1	2	3	4	5	6	7	8	9	10	
9. Heavy pain	0	1	2	3	4	5	6	7	8	9	10	
10. Tender	0	1	2	3	4	5	6	7	8	9	10	
11. Splitting pain	0	1	2	3	4	5	6	7	8	9	10	
12. Tiring-exhausting	0	1	2	3	4	5	6	7	8	9	10	
13. Sickening	0	1	2	3	4	5	6	7	8	9	10	
14. Fearful	0	1	2	3	4	5	6	7	8	9	10	
15. Punishing-cruel	0	1	2	3	4	5	6	7	8	9	10	
16. Electric-shock pain	0	1	2	3	4	5	6	7	8	9	10	
17. Cold-freezing pain	0	1	2	3	4	5	6	7	8	9	10	
18. Piercing	0	1	2	3	4	5	6	7	8	9	10	
19. Pain caused by light touch	0	1	2	3	4	5	6	7	8	9	10	
20. Itching	0	1	2	3	4	5	6	7	8	9	10	
21. Tingling or "pins and needles"	0	1	2	3	4	5	6	7	8	9	10	
22. Numbness	0	1	2	3	4	5	6	7	8	9	10	

TKA/THA NERVE BLOCK STUDY

Form SURG

Surgical Parameters

Final 05/27/2016

Study ID _____

Staff Initials _____

Form Date ____/____/____

1. Date of Admission: ____/____/____

2. Date of Surgery: ____/____/____

3. What type of surgery was performed?

☐ Conventional TKA (should typically be cemented)

☐ Conventional THA (should not typically be cemented)

☐ Other: _____

☐ Cemented

☐ Cementless

4. The total joint replacement is primarily due to:

☐ Osteoarthritis

☐ Inflammatory arthritis (e.g., Rheumatoid Arthritis)

☐ Recent trauma (e.g., fracture)

☐ Idiopathic necrosis/avascular necrosis

☐ Other: _____

5. Was there a complication during surgery (e.g. periprosthetic fracture) that required additional/change in surgical procedure?

☐ Yes

☐ No

If yes, comment: _____

If the periprosthetic fracture or other complication is deemed sufficient to disrupt postoperative physical therapy planning per protocol, then notify the coordinator to withdraw the patient.

6. Was the PCL preserved (TKA only)? ☐ Yes ☐ No ☐ N/A (hip)

7. Operating surgeon: _____

☐ Chief Resident

☐ Super-Chief

8. Attending surgeon: _____

TKA/THA NERVE BLOCK STUDY		
Form SURG	Surgical Parameters	Final 05/27/2016
Study ID _____	Staff Initials _____	Form Date ____/____/____

For the following questions, respond only according to the surgery performed:

9. Number of [TKA/THA] performed by the operating surgeon per year:

- ☐ 0 to 50
- ☐ 51 to 100
- ☐ 101 to 150
- ☐ 151 to 200
- ☐ above 200

10. Operating surgeon's years of experience performing [TKA/THA]:

- ☐ 0 to 5
- ☐ 6 to 10
- ☐ 11 to 15
- ☐ 16 to 20
- ☐ over 21

☐ CPRS Surgical Op note generated

TKA/THA NERVE BLOCK STUDY		
Form WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index, Version LK3.1	Final 04/12/2016
Study ID _____ Staff Initials _____ Form Date ____/____/____		

Visit: ☐ Baseline ☐ Week 6 Time: _____

Section A

INSTRUCTIONS TO PATIENTS:

Think about the pain you felt in your (knee or hip) caused by your arthritis during the last 48 hours.

QUESTION: How much pain have you had...

1. when walking on a flat surface?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

2. when going up or down stairs?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

3. at night while in bed? (that is – pain that disturbs your sleep)

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

4. while sitting or lying down?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

5. while standing?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

Section B

INSTRUCTIONS TO PATIENTS:

Think about the stiffness (not pain) you felt in your (knee or hip) caused by your arthritis during the last 48 hours.

6. How **severe** has your stiffness been **after you first woke up** in the morning?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

7. How severe has your stiffness been after sitting or lying down or while resting **later in the day**?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

TKA/THA NERVE BLOCK STUDY		
Form WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index, Version LK3.1	Final 04/12/2016
Study ID _____	Staff Initials _____	Form Date ____/____/____

Section C

INSTRUCTIONS TO PATIENTS:

Think about the difficulty you had in doing the following daily physical activities caused by the arthritis in your (knee or hip) during the last 48 hours. By this we mean **your ability to move around and take care of yourself**.

QUESTION: How much difficulty have you had...

8. when going down stairs?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

9. when going up the stairs?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

10. when getting up from a sitting position?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

11. while standing?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

12. when bending to the floor?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

13. when walking on a flat surface?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

14. getting in or out of a car, or getting on or off a bus?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

15. while going shopping?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

TKA/THA NERVE BLOCK STUDY		
Form WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index, Version LK3.1	Final 04/12/2016
Study ID _____ Staff Initials _____ Form Date ____/____/____		

QUESTION: **How much difficulty have you had...**

16. when putting on your socks or panty hose or stockings?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

17. when getting out of bed?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

18. when taking off your socks or panty hose or stockings?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

19. while lying in bed?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

20. when getting in or out of the bathtub?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

21. while sitting?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

22. when getting on or off the toilet?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

23. while doing heavy household chores?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

24. while doing light household chores?

none	mild	moderate	severe	extreme
☐	☐	☐	☐	☐

Study Calendar

From Protocol Version 06/10/16

[illegible]

	Screening Visit	Baseline Visit	Day of surgery		Post-Op Day 1	Post-Op Day 2	Post-Op Day 3	Post-Op Day 4	Post-Op Day 5	Post-Op Week 2 Follow-Up Visit ^d	Post-Op Week 6 Follow-Up Visit ^{c, e}
			Pre-Procedure	Post-procedure							
Questionnaires											
SFMPQ-2 ^b		X	X	X	X	X	X	X	X		X
DVPRS		X	X	X						X	X
DVPRS- in hospital ^b					X	X	X	X	X		
ORSDS ^b		X			X	X	X	X	X		
QOR-15 ^b		X			X	X	X	X	X		X
WOMAC		X									X
SF-8 ^b			X		X	X	X	X	X	X	
SF-36		X									X
Falls Questionnaire		X			X	X	X	X	X		X

a. The screening visit and baseline visit can be completed on the same day.

b. On post-op hospital days and post-op week 6 follow-up visits, these questionnaires will be completed before the subject has their first physical therapy session for the day.

c. If a patient decides to withdraw from the study after having their surgery, or is withdrawn by the study team during or after their surgery, they will be asked to complete the Week 6 Post-op follow-up visit.

d. The Week 2 Post-op follow-up visit will occur with the patient's already scheduled standard of care 2 week post-op orthopedic visit.

e. The Week 6 Post-op follow up visit will be scheduled to coincide with the patient's standard of care 6 week post-op orthopedic visit.

f. Patient must pass the standing balance test first, before the single leg balance test can be attempted.

g. The opioid consumption log should be completed within 7 days of the patient being discharged.

**NERVE BLOCK STUDY PARTICIPANT POST-OP WEEK 2 ORTHO
CLINIC/RESEARCH VISIT
SOCIAL WORK AND TRANSPORTATION COMMUNICATION
Version 1 – 09/23/16 (Final)**

One week prior to study participant's scheduled surgery date, Study Coordinator will send an encrypted email to the Inpatient Social Work Manager (Anita Pasquale/Surrogate) with the name(s) and scheduled date(s) of surgery for TKA/THA patients that are enrolled in the NERVE BLOCK Study.

After surgery is complete, Study Coordinator will confirm with Inpatient Social Work Manager via encrypted email that patient remains on study.

On Post-Op Day 1, a note will be placed on the floor chart stating that the patient is a participant in the NERVE BLOCK Study.

Inpatient Social Work Manager will advise patient Case Worker to include Study Coordinator as a Cosigner on CPRS Notes that concern patient discharge planning.

Study Coordinator will schedule study participant's Post-Op Week 2 Ortho Clinic Appointment and Research Visit either on the day of discharge or within three days of discharge.

Study Coordinator will confirm via telephone with study participant the day and time of their Post-Op Week 2 Ortho Clinic/Research Visit three to five days prior to scheduled appointment.

If it is known that a study participant will remain in a non-VA facility at time of Post-Op Week 2 Ortho Clinic/Research Visit and is $\geq 30\%$ Service Connected, Beneficiary Travel can be arranged through the Transportation and Fleet Operations Department Transportation Assistants at (412) 360-3620 or (412) 360-6783.

**NERVE BLOCK STUDY PARTICIPANT POST-OP WEEKS 2 AND 6 ORTHO
CLINIC/RESEARCH VISIT SCHEDULING**

Version 1 – 09/23/16 (Final)

During Baseline Research Visit, study participant will be advised that Study Coordinator will be involved in making their Post-Op Ortho Clinic and Research Visit appointments.

On Post-Op Day 1, a note will be placed on the floor chart stating that the patient is a participant in the NERVE BLOCK Study and that the Study Coordinator will schedule Post-Op Week 2 Ortho Clinic Appointment.

Study Coordinator will remind study participant that Post-Op Ortho Clinic/Research Visits will be scheduled by the Study Coordinator.

Study Coordinator will schedule study participant's Post-Op Week 2+ Ortho Clinic Appointment and Research Visit either on the day of discharge or within three days of discharge. Both visits will take place in the Ortho Clinic Exam/Waiting Room Area.

Study Coordinator will confirm via telephone with study participant the day and time of their Post-Op Week 2 Ortho Clinic/Research Visit three to five days prior to scheduled appointment.

One business day prior to scheduled appointment, Study Coordinator will send via encrypted email, a list of study participants scheduled for Post-Op Week 2 Ortho Clinic Appointments to MSA Supervisor, Surgery Services (or surrogate).

MSA Supervisor, Surgery Services will direct MSAs to advise Study Coordinator of study participant's arrival on day of appointment.

Study Coordinator will meet with study participant in the Ortho Clinic Exam/Waiting Room Area to complete Post-Op Week 2 Questionnaires (SF8 and DVPRS), CON MEDS form and schedule Post-Op Week 6++ Ortho Clinic Appointment and Research Visit.

Study Coordinator will confirm via telephone with the study participant the Week 6 Post-Op Ortho Clinic Appointment/Research Visit three to five days prior to scheduled appointment and will arrange transportation to the Research Office Building, if necessary.

One business day prior to scheduled appointment, Study Coordinator will send via encrypted email, a list of study participants scheduled for Post-Op Week 6 Ortho Clinic Appointments to MSA Supervisor, Surgery Services.

MSA Supervisor, Surgery Services will direct MSAs to advise Study Coordinator of study participants' arrival on day of appointment.

Study Coordinator will meet the study participant at the Ortho Clinic and, if necessary, escort study participant to Hero's Hall for transportation or directly to the Research Office Building.

+ Requested date range may fluctuate from 7 - 10 days to 4 weeks. Ortho will make final recommendation at the time of discharge

++ Requested date range may fluctuate from 6 weeks to 3 months based on date of Post-Op Week 2 Visit.

NERVE BLOCK Patient Information Communication and Study Form Distribution Procedures

Version 1 – 05/20/16 (Final)

- Participant recruitment will be tracked by the Study Coordinator (SC), and participants will be assigned two identification (ID) numbers:

Patient ID (PID) = Number assigned to patient at time of consent

Study ID (SID) = Number assigned to patient at time of randomization

- Communication about patient study status and scheduled visits will always include their SID number.
- The PID and SID lists will be updated daily and located on the Nerve Block Study Shared Drive (\\vhaphthshare\Nerve_Block_Study\). These lists will be viewable by designated study staff when signed in to the VA Network. A hard copy/binder containing this information will also be available in a locked cabinet in the Clinical Trials Center (CTC) in the Research Office Building (ROB).
- The Nerve Block Study Schedule in Outlook Calendar will be updated daily, noting SIDs and scheduled visits. The Schedule will only be viewable by designated study staff when signed in to the VA Network.

Examples: NERVE BLOCK PATIENT: 10651001/Post OpDay 2
NERVE BLOCK PATIENT: 11621332/BASELINE

- At the end of each business day, two emails will be sent by the SC:
 1. an **unencrypted** email noting the tentative next day's patients' schedules with only SIDs and scheduled visits will be sent to the Pitt Physical Therapy (PT) Staff.
 2. an **encrypted** email noting the tentative next day's patients' schedules that will include patient names, SIDs and scheduled visits will be sent to the Principal Investigator [PI], Co-Investigators [Co-Is], VA and Pitt PT staffs, and the Investigational Drug Service [IDS]]. This communication will only be viewable when signed in to the VA Network.

NERVE BLOCK Patient Information Communication and Study Form Distribution Procedures

Version 1 – 05/20/16 (Final)

3. Communication by the Pitt PT staff regarding weekend patient discharge(s) will be sent via **encrypted** email (i.e., within the VA email network) to the SC.

Monday through Friday Form Distribution:

1. Between 7:00 and 7:30AM, the SC will place two Clinical Exam (CEX) Forms (AM/PM PT Visits) and one Falls-IH Form (PM PT Visit) per study participant into folder(s) identified by Patient Name and SID in a locked file cabinet located in the PT Department, Room 2W113.
2. As necessary, SC will also pick up all completed forms, and/or remove patient folder(s) from previous day(s) if patient(s) have been discharged.

Morning PT Session:

1. Prior to beginning the AM PT sessions, the VA PT Staff will locate the patient's/patients' folder(s).
2. Appropriate assessments and treatments will be completed with the patient and documentation about the session will be made on the CEX Form.
3. The completed CEX Form will be returned to its original folder and the folder returned to the locked file cabinet in Room 2W113.

Afternoon PT Session:

1. Prior to beginning PM PT assessments and treatments, the Pitt PT Staff will locate the patient's/patients' folder(s).
2. Appropriate assessments and treatments will be completed with the patient and documentation about the session will be made on the CEX Form.
3. The FALLS-IH Form will be completed.
4. Collected data from the CEX and FALLS-IH Forms will be entered into REDCap (both AM and PM PT sessions).
5. After REDCap data entry, the completed CEX and FALLS-IH Forms will be returned to their original folder and the folder returned to the locked file cabinet in Room 2W113.

NERVE BLOCK Patient Information Communication and Study Form Distribution Procedures

Version 1 – 05/20/16 (Final)

Weekend Questionnaires and Form Distribution:

Friday Afternoon:

4. The SC will place two copies of daily patient questionnaires⁺ (Saturday/Sunday AM), four CEX Forms (Saturday and Sunday AM and PM PT sessions) and two FALLS-IH Forms (on Weekends, completed during AM PT sessions) per patient in folder(s) identified by Patient Name and SID in the locked file cabinet located in Room 2W113.

Saturday/Sunday Morning PT Session:

1. Prior to beginning AM PT assessments and treatments, the Pitt PT Staff will locate the patient's/patients' folder(s).
2. Pitt PT staff will have the patient complete daily questionnaires.
3. Upon completion of the questionnaires, appropriate assessments and treatments will be completed with the patient, and documentation about the session will be made on the CEX Form.
4. The FALLS-IH Form will be completed.
5. Collected data from the completed CEX and FALLS-IH Forms ONLY will be entered into REDCap (Saturday: AM session only; Sunday: Saturday PM and Sunday AM sessions; Sunday PM session data to be entered on Monday). Daily patient questionnaire data will be entered into REDCap by SC during the week.
6. After REDCap data entry, the completed CEX and FALLS-IH Forms will be returned to their original folder, and the folder returned to the locked file cabinet in Room 2W113.

Saturday/Sunday Afternoon PT Session:

1. Prior to beginning PM PT assessments and treatments, VA Occupational Therapy ([OT] - Saturday/PT - Sunday) staff will locate patient's/patients' folder(s).
2. Appropriate assessments and treatments will be completed and documentation about the session will be made on the CEX Form.

**NERVE BLOCK Patient Information Communication
and Study Form Distribution Procedures**

Version 1 – 05/20/16 (Final)

3. The completed CEX will be returned to its original folder and the folder returned to the locked file cabinet in Room 2W113.

SFMPQ2 (Short-Form McGill Pain Questionnaire 2)

SF8 (SF-8 Health Survey)

QOR15 (Quality of Recovery)

ORSDS (Opioid-Related Symptom Distress Scale)

DVPRS-IH (Defense and Veterans Pain Rating Scale – In Hospital)

ADMINISTRATIVE INFO ONLY

Nerve Block Study

Original

Block: # Assignment: FIRST - FIFTH

Participant

8 Digit Number Comprised of:

Surgery Type:

1 = TKA, 2 = THA

Diabetes presence:

0 = Absent, 1 = Present

Age Classification:

6 = ≤69yo, 7 = >69yo

Drug Assignment:

1 through 5

4 Digit Enrollment #:

1001 through 9999

NERVE BLOCK PREPARATION INSTRUCTIONS AND ACCOUNTABILITY FORM

SUBJECT RANDOMIZED TO BUPIVACAINE AND CLONIDINE-BUPRENORPHINE-DEXAMETHASONE	VA PITTSBURGH Dispensing area: UD-SDPU
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Subject Name	Last 4 digits SS	AGE of PARTICIPANT ☐ ≤ 69 y ☐ > 69 y <i>Max 85 years</i>	
Randomization Number	PROCEDURE ☐ Total KNEE Replacement ☐ Total HIP Replacement	Diabetes PRESENT	Diabetes ABSENT X
☐ the Nerve Block Syringes were prepared according to the standard procedures noted on the mixing instructions PREPARED BY:		DATE PREPARED	TIME PREPARED

STEP 1: OBTAIN SUPPLIES

ITEM	QUANTITY NEEDED	OBTAIN FROM
BUPIVACAINE 0.5% 30mL VIAL	1 VIAL	OMNICELL CABINET SELECT KIT "INV BUPIVACAINE+CBD- NERVE BLOCK STUDY"
DEXAMETHASONE 10mg/1mL SDV VIAL	1 VIAL	
BUPRENORPHINE 300mcg/1mL VIAL	2 VIALS	
0.9% SODIUM CHLORIDE 20mL VIAL	2 VIALS	
CLONIDINE 30mcg/0.3mL SYRINGE ***USE ONLY 25mcg/0.25mL***	2 SYRINGES	SDPU REFRIGERATOR

STEP 2: PRIOR TO MIXING

- WIPE BLOCK CART MIXING SURFACE WITH DISINFECTANT WIPE
- DON HAT AND MASK; APPLY PURELL TO HANDS
- OBTAIN STERILE SYRINGES AND NEEDLES FROM NERVE BLOCK CART SUPPLIES
- MIX AT A BLOCK CART THAT IS OUT OF RANGE OF (I) THE STUDY PATIENT AND THE STUDY COORDINATOR, (II) THE ANESTHESIA AND/OR ORTHOPEDIC PERSONNEL OF RECORD, AND (III) THE RN NERVE BLOCK SPECIALIST AND/OR SDPU RN TEAM

STEP 3: MIXING

- **WITHDRAW THE REQUIRED VOLUMES NOTED BELOW**
- **PREPARE A TOTAL OF TWO SYRINGES; TOTAL VOLUME OF EACH SYRINGE = 20mL**
- **LABEL EACH SYRINGE WITH THE APPROPRIATE PROVIDED LABELS**
- **Place all USED vials, syringes and needles in the appropriate disposal container as per standard procedures**

- **DOCUMENT ON THE FRONT SIDE OF THIS FORM THE DATE AND TIME OF PREPARATION AND NAME OF MIXER**
- **PLACE COMPLETED FORM, and OPENED WHITE RANDOMIZATION ENVELOPE IN THE PROVIDED MANILA ENVELOPE, SEAL, and RETURN TO STUDY OR PHARMACY STAFF.**

NON-DIABETIC						
COMPLETE INFORMATION BELOW			PREPARE TWO 20ML SYRINGES		FOR L2-L4 BLOCK SYRINGE	FOR L4-S3 BLOCK SYRINGE
DRUG	# VIALS OR SYRINGES	MANUFACTURER	LOT #	EXPIRATION DATE	QUANTITY NEEDED	
BUPIVACAINE 0.5% 30 mL vial	1 VIAL				10mL	4mL
DEXAMETHASONE 10mg/1mL	1 VIAL				0.1mL	0.1mL
BUPRENORPHINE 300mcg/1mL	2 VIALS				1mL	1mL
CLONIDINE 30mcg/0.3mL	2 SYR				0.25mL	0.25mL
0.9% SODIUM CHLORIDE 20 mL	2 VIALS				8.65mL	14.65mL
FINAL TOTAL VOLUME OF SYRINGE					20mL	20mL
FINAL BUPIVACAINE CONCENTRATION					0.25%	0.1%

***** NOTE: THE NERVE BLOCK SYRINGES MUST BE USED WITHIN 60 MINUTES OF PREPARATION******

AFFIX one copy of the SYRINGE LABELS to each of these boxes

NERVE BLOCK PREPARATION INSTRUCTIONS AND ACCOUNTABILITY FORM

SUBJECT RANDOMIZED TO BUPIVACAINE AND CLONIDINE-BUPRENORPHINE-DEXAMETHASONE	VA PITTSBURGH Dispensing area: UD-SDPU
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Subject Name	Last 4 digits SS	AGE of PARTICIPANT ☐ ≤ 69 y ☐ > 69 y <i>Max 85 years</i>	
Randomization Number	PROCEDURE ☐ Total KNEE Replacement ☐ Total HIP Replacement	Diabetes PRESENT X	Diabetes ABSENT
☐ the Nerve Block Syringes were prepared according to the standard procedures noted on the mixing instructions PREPARED BY:		DATE PREPARED	TIME PREPARED

STEP 1: OBTAIN SUPPLIES

ITEM	QUANTITY NEEDED	OBTAIN FROM
BUPIVACAINE 0.5% 30mL VIAL	1 VIAL	OMNICELL CABINET SELECT KIT "INV BUPIVACAINE+CBD- NERVE BLOCK STUDY"
DEXAMETHASONE 10mg/1mL SDV VIAL	1 VIAL	
BUPRENORPHINE 300mcg/1mL	2 VIALS	
0.9% SODIUM CHLORIDE 20mL VIAL	2 VIALS	
CLONIDINE 30mcg/0.3mL SYRINGE ***USE ONLY 25mcg/0.25mL***	2 SYRINGES	SDPU REFRIGERATOR

STEP 2: PRIOR TO MIXING

- WIPE BLOCK CART MIXING SURFACE WITH DISINFECTANT WIPE
- DON HAT AND MASK; APPLY PURELL TO HANDS
- OBTAIN STERILE SYRINGES AND NEEDLES FROM NERVE BLOCK CART SUPPLIES
- MIX AT A BLOCK CART THAT IS OUT OF RANGE OF (I) THE STUDY PATIENT AND THE STUDY COORDINATOR, (II) THE ANESTHESIA AND/OR ORTHOPEDIC PERSONNEL OF RECORD, AND (III) THE RN NERVE BLOCK SPECIALIST AND/OR SDPU RN TEAM

STEP 3: MIXING

- WITHDRAW THE REQUIRED VOLUMES NOTED BELOW
- PREPARE A TOTAL OF TWO SYRINGES; TOTAL VOLUME OF EACH SYRINGE = 20mL
- LABEL EACH SYRINGE WITH THE APPROPRIATE PROVIDED LABEL
- Place all USED vials, syringes and needles in the appropriate disposal container as per standard procedures

- DOCUMENT ON THE FRONT SIDE OF THIS FORM THE DATE AND TIME OF PREPARATION AND NAME OF MIXER
- PLACE COMPLETED FORM, and OPENED WHITE RANDOMIZATION ENVELOPE IN THE PROVIDED MANILA ENVELOPE, SEAL, and RETURN TO STUDY OR PHARMACY STAFF.

DIABETIC						
PREPARE TWO 20mL SYRINGES						
COMPLETE THE INFORMATION BELOW					FOR L2-L4 BLOCK SYRINGE	FOR L4-S3 BLOCK SYRINGE
DRUG	# VIALS OR SYRINGES	MANUFACTURER	LOT #	EXPIRATION DATE	QUANTITY NEEDED	
BUPIVACAINE 0.5% 30 mL vial	1 VIAL				8mL	4mL
DEXAMETHASONE 10mg/1mL	1 VIAL				0.1mL	0.1mL
BUPRENORPHINE 300mcg/1mL	2 VIALS				1mL	1mL
CLONIDINE 30mcg/0.3mL	2 SYR				0.25mL	0.25mL
0.9% SODIUM CHLORIDE 20 mL	2 VIALS				10.65mL	14.65mL
FINAL TOTAL VOLUME OF SYRINGE					20mL	20mL
FINAL BUPIVACAINE CONCENTRATION					0.2%	0.1%

***** NOTE: THE NERVE BLOCK SYRINGES MUST BE USED
WITHIN 60 MINUTES OF PREPARATION*****

**AFFIX one copy of
the SYRINGE LABELS
to each of these boxes**

NERVE BLOCK PREPARATION INSTRUCTIONS AND ACCOUNTABILITY FORM

SUBJECT RANDOMIZED TO *** BUPIVACAINE ONLY****	VA PITTSBURGH Dispensing area: UD-SDPU
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Subject Name	Last 4 digits SS	AGE of PARTICIPANT ☐ ≤ 69 y ☐ > 69 y <i>Max 85 years</i>	
Randomization Number	PROCEDURE ☐ Total KNEE Replacement ☐ Total HIP Replacement	Diabetes PRESENT	Diabetes ABSENT X
☐ the Nerve Block Syringes were prepared according to the standard procedures noted on the mixing instructions PREPARED BY:		DATE PREPARED	TIME PREPARED

STEP 1: OBTAIN SUPPLIES

ITEM	QUANTITY NEEDED	OBTAIN FROM
BUPIVACAINE 0.5% 30mL VIAL	1 VIAL	OMNICELL CABINET SELECT KIT "INV BUPIVACAINE ONLY- NERVE BLOCK STUDY"
0.9% SODIUM CHLORIDE 20mL VIAL	2 VIALS	

STEP 2: PRIOR TO MIXING

- WIPE BLOCK CART MIXING SURFACE WITH DISINFECTANT WIPE
- DON HAT AND MASK; APPLY PURELL TO HANDS
- OBTAIN STERILE SYRINGES AND NEEDLES FROM NERVE BLOCK CART SUPPLIES
- MIX AT A BLOCK CART THAT IS OUT OF RANGE OF (I) THE STUDY PATIENT AND THE STUDY COORDINATOR, (II) THE ANESTHESIA AND/OR ORTHOPEDIC PERSONNEL OF RECORD, AND (III) THE RN NERVE BLOCK SPECIALIST AND/OR SDPU RN TEAM

STEP 3: MIXING

- **WITHDRAW THE REQUIRED VOLUMES NOTED BELOW**
- **PREPARE A TOTAL OF TWO SYRINGES; TOTAL VOLUME OF EACH SYRINGE = 20ML**
- **LABEL EACH SYRINGE WITH THE APPROPRIATE PROVIDED LABEL**
- **Place all USED vials, syringes and needles in the appropriate disposal container as per standard procedures**

- **DOCUMENT ON THE FRONT SIDE OF THIS FORM THE DATE AND TIME OF PREPARATION AND NAME OF MIXER**
- **PLACE COMPLETED FORM, and OPENED WHITE RANDOMIZATION ENVELOPE IN THE PROVIDED MANILA ENVELOPE, SEAL, and RETURN TO STUDY OR PHARMACY STAFF.**

NON-DIABETIC						
PREPARE TWO 20mL SYRINGES						
COMPLETE INFORMATION BELOW					FOR L2-L4 BLOCK SYRINGE	FOR L4-S3 BLOCK SYRINGE
DRUG	# VIALS OR SYRINGES	MANUFACTURER	LOT #	EXPIRY	QUANTITY NEEDED	
BUPIVACAINE 0.5% 30 mL vial	1 VIAL				10mL	4mL
0.9% SODIUM CHLORIDE 20 mL	2 VIALS				10mL	16mL
FINAL TOTAL VOLUME OF SYRINGE					20mL	20mL
FINAL BUPIVACAINE CONCENTRATION					0.25%	0.1%

***** NOTE: THE NERVE BLOCK SYRINGES MUST BE USED
WITHIN 60 MINUTES OF PREPARATION*****

	AFFIX one copy of the SYRINGE LABELS to each of these boxes	
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NERVE BLOCK PREPARATION INSTRUCTIONS AND ACCOUNTABILITY FORM

SUBJECT RANDOMIZED TO ***BUPIVACAINE ONLY***	VA PITTSBURGH Dispensing area: UD-SDPU
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Subject Name	Last 4 digits SS	AGE of PARTICIPANT ☐ ≤ 69 y ☐ > 69 y <i>Max 85 years</i>	
Randomization Number	PROCEDURE ☐ Total KNEE Replacement ☐ Total HIP Replacement	Diabetes PRESENT X	Diabetes ABSENT
☐ the Nerve Block Syringes were prepared according to the standard procedures noted on the mixing instructions PREPARED BY:		DATE PREPARED	TIME PREPARED

STEP 1: OBTAIN SUPPLIES

ITEM	QUANTITY NEEDED	OBTAIN FROM
BUPIVACAINE 0.5% 30mL VIAL	1 VIAL	OMNICELL CABINET SELECT KIT "INV BUPIVACAINE ONLY- NERVE BLOCK STUDY"
0.9% SODIUM CHLORIDE 20mL VIAL	2 VIALS	

STEP 2: PRIOR TO MIXING

- WIPE BLOCK CART MIXING SURFACE WITH DISINFECTANT WIPE
- DON HAT AND MASK; APPLY PURELL TO HANDS
- OBTAIN STERILE SYRINGES AND NEEDLES FROM NERVE BLOCK CART SUPPLIES
- MIX AT A BLOCK CART THAT IS OUT OF RANGE OF (I) THE STUDY PATIENT AND THE STUDY COORDINATOR, (II) THE ANESTHESIA AND/OR ORTHOPEDIC PERSONNEL OF RECORD, AND (III) THE RN NERVE BLOCK SPECIALIST AND/OR SDPU RN TEAM

STEP 3: MIXING

- **WITHDRAW THE REQUIRED VOLUMES NOTED BELOW**
- **PREPARE A TOTAL OF TWO SYRINGES; TOTAL VOLUME OF EACH SYRINGE = 20mL**
- **LABEL EACH SYRINGE WITH THE APPROPRIATE PROVIDED LABEL**
- **Place all USED vials, syringes and needles in the appropriate disposal container as per standard procedures**

- **DOCUMENT ON THE FRONT SIDE OF THIS FORM THE DATE AND TIME OF PREPARATION AND NAME OF MIXER**
- **PLACE COMPLETED FORM, and OPENED WHITE RANDOMIZATION ENVELOPE IN THE PROVIDED MANILA ENVELOPE, SEAL, and RETURN TO STUDY OR PHARMACY STAFF.**

DIABETIC						
COMPLETE INFORMATION BELOW			PREPARE TWO 20ML SYRINGES		FOR L2-L4 BLOCK SYRINGE	FOR L4-S3 BLOCK SYRINGE
DRUG	# VIALS OR SYRINGES	MANUFACTURER	LOT #	EXPIRY	QUANTITY NEEDED	
BUPIVACAINE 0.5% 30 mL vial	1 VIAL				8mL	4mL
0.9% SODIUM CHLORIDE 20 mL	2 VIALS				12mL	16mL
FINAL TOTAL VOLUME OF SYRINGE					20mL	20mL
FINAL BUPIVACAINE CONCENTRATION					0.2%	0.1%

***** NOTE: THE NERVE BLOCK SYRINGES MUST BE USED
WITHIN 60 MINUTES OF PREPARATION******

AFFIX one copy of the SYRINGE LABELS to each of these boxes		
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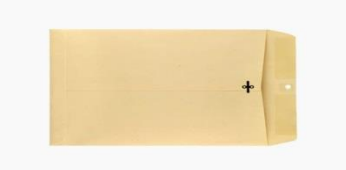
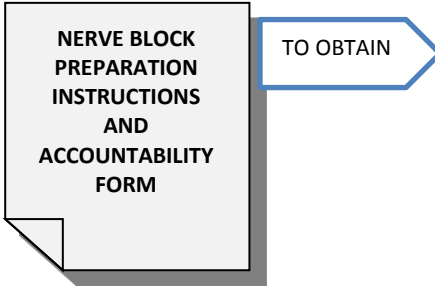
NERVE BLOCK STUDY RANDOMIZATION# _____ SYRINGE FOR L2-L4 BLOCK Prep date: _____ time _____ Affix to syringe	NERVE BLOCK STUDY RANDOMIZATION# _____ SYRINGE FOR L2-L4 BLOCK Prep date: _____ time _____ Attach to prep/accountability form
--	--

EXAMPLE:
THIS COULD BE BLUE COLOR

NERVE BLOCK STUDY RANDOMIZATION# _____ SYRINGE FOR L4-S3 BLOCK Prep date: _____ time _____ Affix to syringe	NERVE BLOCK STUDY RANDOMIZATION# _____ SYRINGE FOR L4-S3 BLOCK Prep date: _____ time _____ Attach to prep/accountability form
--	--

EXAMPLE:
THIS COULD BE GREEN COLOR

RETURN ENVELOPE	
4-DRUG NERVE BLOCK VERSUS PLAIN LOCAL ANESTHETIC FOR KNEE AND HIP ARTHROPLASTY ANALGESIA IN VETERANS	IRB# PRO 1357
PI: Brian Williams, MD	Study Coordinator: Karen Gilbert
RANDOMIZATION NUMBER:	

STEP 1	❖ OPEN SEALED RANDOMIZATION ENVELOPE 	RETRIEVE THE ENCLOSED FORM 	TREATMENT ASSIGNMENT This Form will indicate: BUPIVACAINE OR BUPIVACAINE + C-B-D
STEP 2	❖ FOLLOW THE PREPARATION INSTRUCTIONS ON FORM ❖ LABEL THE TWO NERVE BLOCK SYRINGES		
STEP 3	❖ REMEMBER TO AFFIX ONE COPY EACH OF THE SYRINGE LABELS TO THE FORM		
STEP 3	❖ REMEMBER TO COMPLETE AND SIGN THE FORM		
STEP 4	IN THE PROVIDED RETURN ENVELOPE PLACE THE FOLLOWING ITEMS ▪ <u>COMPLETED</u> NERVE BLOCK PREP INSTRUCTIONS AND ACCOUNTABILITY FORM ▪ OPENED RANDOMIZATION ENVELOPE		
STEP 5	**SEAL THE ENVELOPE** WITH THE ABOVE ENCLOSED CONTENTS		
STEP 6	RETURN THE <u>SEALED ENVELOPE</u> to A STUDY INVESTIGATOR		

PLEASE COMPLETE:

- 1) I attest that the ENVELOPE provided containing the NERVE BLOCK PREPARATION and ACCOUNTABILITY form was SEALED prior to my opening the envelope
- 2) I attest that the form noted above was completed by me and no other person involved with the study or involved with the clinical care of the study participant observed the randomization materials or the nerve block preparation process.

Printed name _____

Signature _____ Date: ____/____/____

IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT THE INVESTIGATIONAL DRUG SERVICE	Shirley Podnar, PharmD 412-360-3260 Pager: 1711	Meghan Tamburino, CPhT 412-360-3792 Pager: 1710
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CLINICAL EXAMINATION

General Instructions

It is recommended that participants wear loose clothing and flat comfortable shoes or tennis shoes for both acute and clinic visits. For the tests that require standing and walking, it is recommended that shoes are worn; however, well-fitting hospital socks with adequate grips on bottom are permissible for walking and standing assessments. It is recommended that the research coordinator advise participants of these apparel recommendations when scheduling the baseline visit. The research coordinator and PT conducting the baseline assessment should reiterate these recommendations at baseline visit.

If at any time during testing, the tester feels the participant is unsafe, end the testing. For the crude sensation, range of motion, and active straight leg raise tests, the non-operative side is tested first, and the operative side is tested next. For the timed tests, the time is recorded to the nearest hundredth of a second (two decimals). The testers will attempt to complete the clinical examination form in the order that is on the form. This will be done because the order of testing could impact participant's performance.

Prior to starting initial assessment, the therapist should access CPRS to determine weight bearing status, activity orders, precautions, and contraindications. Before the clinical exam, complete the top portion of the clinical exam form and assess resting pain (from 0 to 10) in the knee (for those in total knee replacement group) or hip (for those in total hip replacement group) and record it. Blood pressure will be taken in standing position as the evaluation and treatment session proceeds. Standing blood pressure must be taken prior to commencing gait assessment and standing therapeutic exercise.

Any Adverse Events, Serious Adverse Events, or Protocol deviations should be communicated to the Study Coordinator within IRB guidelines.

Equipment and communal room cleaning should be performed per VAPHS Cleaning Guidelines. After patient contact, equipment, like goniometers, blood pressure cuffs, oxygen saturation finger sensors, and stethoscopes, should be cleaned with PDI Wipes or alcohol as appropriate. In communal areas, like ROB treatment rooms, a) pillow cases should be changed and b) linens should be changed and/or treatment tables cleaned as appropriate after patient use.

Vital Guidelines

When patient's vitals fall outside the guidelines below, notify the doctor (referred to as HO or House Officer) and patient nurse immediately. Furthermore, call a Code when medically appropriate. VA codes and their descriptions are included in Appendix A. To call a code, you will dial 911 from any hardwired telephone; tell the operator the condition; then give the facility, building, floor and room number; afterwards, make sure to listen to the overhead message to ensure the proper area and code is announced.

Vitals Order:	Call HO for:
* Blood Pressure systolic greater than	200
* Blood Pressure systolic less than	100
* Blood Pressure diastolic greater than	120
* Heart Rate greater than	120
* Heart Rate less than	60
* Temperature greater than	101 degrees F

Vitals Order:	Call a Code for:
* Blood Pressure systolic	Less than 80 regardless of symptom or complaint

Lab Value Guidelines

Lab Values	No Therapeutic Exercise if:	
Hematocrit	<25% (Normal 42-52%)	
Hemoglobin	<8 (Normal 14-18g/dl)	
White Blood Cells	<5,000+fever (Normal 4.8-11.0k/mm ³)	
Platelets	<25,000 No Progressive Resistance Exercise; <10,000 No Rehab (Normal 150,000 to 450,000 mcL)	
Lab Values	NORMAL	THERAPEUTIC
Prothrombin time (PT)	9.5 to 13 sec	18 to 30 sec
Partial thromboplastin time (PTT)	22 to 36 sec	42.75-115.5 sec
International Normalized Ratio (INR)	0.8 to 1.2	2.0 to 3.0(low dose) / 2.5-3.5 (high dose)
PT and INR= Coumadin PTT= Heparin		

DESCRIPTION OF TESTS

Crude Sensation (*all time points bilaterally*) - Test will be performed in supine position with both ankles placed on bolster or towel with both lower extremities in full extension. Patient's eyes will be closed. L2-4 distribution is tested at anterior thigh and medial anterior lower leg. L5-S3 distribution will be tested at lateral lower leg and foot. Tester asks patient to stay with eyes closed. Tester lightly touches the area on non-operative side first and asks: "Can you feel me touch your leg?" and then lightly touches the operative side and asks "Do you feel this?" "Does this feel the same, more, or less as the other side?" Tester records if sensation is normal or diminished/absent.

Range of Motion (ROM) (*all time points bilaterally*) - All ROM measures are assessed with a standard goniometer with the patient in supine on the hospital bed or over a treatment table. For all tests the non-tested lower extremity stays flat over the bed in neutral rotation.

- **Hip ROM - for participants with hip replacement only-** Perform non-operative side first and operative side second.
 - **Flexion**
 - **Active.** Participant is supine with tested hip in neutral position. Initially the knee is extended, but flexion should be allowed as hip flexion continues. The limit of ROM for this test is 90 degrees of hip flexion (surgical precaution). Patient actively brings the hip into flexion without any help from the tester and holds that position while the tester takes the measurement. The center of the goniometer is over the lateral aspect of hip referencing the greater trochanter. The fixed arm of the goniometer is over the lateral midline of pelvis. The moving arm is over the lateral midline of femur referencing femoral lateral epicondyle.

- **Passive.** Tester stabilizes the pelvis to prevent rotation or posterior tilting, and flexes the hip until reaching a firm end feel or patient pain tolerance. The limit of ROM for this test is 90 degrees of hip flexion (surgical precaution). Same position and goniometer placement.
- **Abduction**
 - **Active.** Participant is supine (towards the side of the bed opposite to the tested hip) with tested hip in neutral position and knee extended. Patient actively slides the hip into abduction without any help from the tester and holds that position while the tester takes the measurement. The center of the goniometer is over the anterior superior iliac spine (ASIS). The fixed arm of the goniometer is over an imaginary horizontal line extending from one ASIS to the other ASIS. The moving arm is over the anterior midline of femur referencing the patella midline.
 - **Passive.** Same position and goniometer placement. The tester brings the lower extremity into abduction without allowing pelvis or leg rotation. The tester stops by reaching a firm end feel or patient pain tolerance.
- **Knee ROM – for participants with knee replacement only-** Perform non-operative side first and operative side second.
- **Flexion**
 - **Active.** Participant supine with tested knee in extension. Initially hip in zero degrees of ext, abd, add. Patient actively brings knee into flexion as far as possible sliding the heel of the testing leg on the surface of the bed without any help from the tester. The center of the goniometer is over the lateral epicondyle of femur. The fixed arm of the goniometer is over the lateral midline of femur, referencing greater trochanter. The moving arm of the goniometer is over the lateral midline of fibula, reference lateral malleolus & fibular head.
 - **Passive.** Participant supine with tested knee in extension. Initially hip in zero degrees of ext, abd, add. Tester flexes knee and hip by sliding the heel of tested knee on the bed. Tester stabilizes the femur and bends the knee until reaching a soft tissue end feel or up to patient pain tolerance, whichever comes first. Same position and goniometer placement.
- **Extension**
 - **Active.** A bolster (i.e., folded towel or pillow) is placed under participant ankles so that knee hyperextension can be measured. Patient actively brings knee into maximum extension without any help from the tester. The center of the goniometer is over the lateral epicondyle of femur. The fixed arm of the goniometer is over the lateral midline of femur, referencing greater trochanter. The moving arm of the goniometer is over the lateral midline of fibula, reference lateral malleolus & fibular head. In the case of a flexion contracture, the value is recorded as negative (-). In the case of knee hyperextension, the value is positive (+) and recorded without a sign.
 - **Passive.** Same position and goniometer placement. The tester brings the knee close to full extension and then offers slight posterior pressure over the distal thigh until reaching a capsular end feel or pain tolerance (whichever comes first). In case the participant has a flexion contracture, the value is reported as negative (-). In the case of knee hyperextension, the value is positive (+) and recorded without a sign.

Pain Intensity after ROM tests (all time points) - At the end of ROM test ask the participant to rate the level of pain (from 0 to 10) during ROM. Query about the knee for those in total knee replacement group and hip for those in total hip replacement group.

Straight leg raise test (ACTIVE) (*all time points- bilaterally*) - Perform non-operative side first and operative side second. It assesses the ability to actively lift the lower extremity (LE) off the bed. If the participant is able to lift the LE off the bed at least 20 degrees, mark “Yes”. If not able to lift the LE to that range of motion, mark as “No”.

Knee extension lag (*all time points- bilaterally*) - It is the difference between the value of passive knee extension and knee extension during the active straight leg raise test. If the difference is $\geq 5^\circ$ it represents a knee extension lag and is recorded as “Yes”. If the difference is less than 5° it is recorded as “No”.

Standing Balance Tests (SBTs) (*all time points*) (*****Patient must be able to perform 1 repetition straight leg raise (SLR) post TKA surgery to be able to stand and ambulate without a knee immobilizer. A SLR is defined as no eccentric lowering of the lower leg. If unable to perform 1 repetition SLR then knee immobilizer must be used for all standing and ambulation.***) The SBTs are only performed on those patients who can stand unassisted without the use of a cane or walker. Moreover, the participant stands at arm’s reach of a steady surface in one side (*e.g., bed head/sideboard, grab bar*) and the tester in the other side. There are three (3) balance tests performed at each assessment visit. For each:

1. The tester will ask the participant if they can stand without the device and are willing to try the test. If they reply “yes” the tester can assist them with getting into the correct position for testing.
2. The tester, for each position, will not only describe to the participant what the test is but will also demonstrate the appropriate position of the feet for testing.
3. The participant will get into the proper position while receiving support from the tester.
4. When the participant appears to be steady, ask if they are ready. When they reply “yes”, the tester says “Ready, begin”. The tester begins timing (i.e. starts the stopwatch) once the participant is standing independently without support from the tester. The timing continues until the participant moves their feet, grabs for support, receives support from the tester or the time has elapsed.

Balance test #1 Side-by-Side stand - The participant is requested to stand for 10 seconds with their feet together (or as close as possible) in a side-by-side position. Tester will describe and demonstrate the test. If the participant is unable to hold the side-by-side stand for 10 seconds the tester will not proceed to the other balance tests (i.e. semi-tandem, tandem). If the participant successfully completes the side-by-side test (i.e. holds test for 10 seconds), the tester will continue to the semi-tandem balance test.

Tester Script:

Now I will show you the first movement. (Demonstrate) I want you to try to stand with your feet together, side-by-side, for about 10 seconds. You may use your arms, bend your knees, or move your body to maintain your balance, but try not to move your feet. Try to hold this position until I tell you to stop.

Stand next to the participant to help him/her into the side-by-side position. Provide just enough support to the participant’s arm to prevent loss of balance. When the participant has his/her feet together, ask “Are you ready?” Then let go and begin timing as you say, “Ready, begin.” Stop the stopwatch and say “Stop” after 10 seconds or when the participant steps out of position or grabs your arm or steady surface. If participant is unable to hold the position for 10 seconds, record result and end the test.

Balance test #2 Semi-tandem stand - The participant is requested to place the heel of one foot to the side of the big toe of the other foot. Either foot can be placed in the forward position. The tester is

advised to encourage participant to try both feet in the different positions to see which is the most comfortable. Once the participant decides which foot to place in front and the timing begins – the participant cannot change their mind and repeat the test with the opposite foot in front. If the participant successfully completes the semi-tandem stand (i.e. holds test for 10 seconds), the tester will continue to the tandem test.

Tester Script:

Now I will show you the second movement. (Demonstrate) I want you to try to stand with the side of the heel of one foot touching the big toe of the other foot for about 10 seconds. You may put either foot in front, whichever is more comfortable for you. You may use your arms, bend your knees, or move your body to maintain your balance, but try not to move your feet. Try to hold this position until I tell you to stop.

Stand next to the participant to help him/her into the semi-tandem position. Provide just enough support to the participant's arm to prevent loss of balance. When the participant has his/her feet in place, ask "Are you ready?" Then let go and begin timing as you say "Ready, begin." Stop the stopwatch and say "Stop" after 10 seconds or when the participant steps out of position or grabs your arm or steady surface. If participant is unable to hold the position for 10 seconds, record result and end the Standing Balance Tests.

Balance test #3 Tandem stand - The participant is requested to stand with the heel of one foot placed directly in front of the toes of the other foot. Either foot can be placed in the forward position. The tester is advised to encourage the participant to try both feet in the positions to see which is the most comfortable. Once the participant decides which foot to place in front and the time begins – the participant cannot change their mind and repeat the test with the opposite foot in front.

Tester Script:

Now I will show you the third movement. (Demonstrate) I want you to try to stand with the heel of one foot in front of and touching the toes of the other foot for about 10 seconds. You may put either foot in front, whichever is more comfortable for you. You may use your arms, bend your knees, or move your body to maintain your balance, but try not to move your feet. Try to hold this position until I tell you to stop.

Stand next to the participant to help him/her into the tandem position. Supply just enough support to the participant's arm to prevent loss of balance. When the participant has his/her feet in place, ask "Are you ready?" Then let go and begin timing as you say, "Ready, begin." Stop the stopwatch and say "Stop" after 10 seconds or when the participant steps out of position or grabs your arm or steady surface.

Self-Selected Gait Speed Test (all time points) – This self-selected gait speed test assesses participant's ability to walk 4 meters or 13 feet. For this test, the tester will need a stopwatch, measuring tape and masking tape (hopefully we will be able to have the tape on the floor at all times). The walking course should be set up prior to the assessment visits and the area should be free from clutter and unobstructed and should include at least an extra meter on each end. The tester will mark the start and finish lines on the floor using the masking tape and a construction meter tape to measure the correct distance.

1. The tester will ask the participant whether they feel safe walking a short distance with or without walking device for the test. If they don't, do not perform the gait speed test. A walking device can be used during the walk.
2. Participants are instructed to walk at their usual or normal walking speed (**i.e., as they would normally walk to run errands**) and past the finish line ~1 meter after the finish line. The tester will begin timing when the participant begins to move (not when they say "Ready,

begin”). The tester will stop timing when the first foot crosses the masking tape finish line. The tester will record the time when the participant’s first foot crosses the 4 meter line. It is imperative that the participant’s foot cross the line and not lands on the line as it does not end the test.

3. The tester will write the time on their data sheet and then instruct the participant that they will perform the test again. The participant will walk back to the starting masking tape and repeat the steps for the gait speed test to obtain the second time. Record the fastest time. If unable to repeat the test record the first time and end the gait speed test. If unable to complete the first test mark as not completed.
4. The tester will not walk beside the participant during the gait speed test, as this may set a pace for the participant, but rather slightly behind and to the side and outside of the participant’s visual field. For those that normally use a walking device, it is recommended that close attention be paid to these individuals during the test to prevent falling.
5. If the tester has issues with the stopwatch, repeat the test.

Pain Intensity prior to FIM (*all time points*) – Prior to gait and stair FIM assessment ask the participant to rate the current level of pain (from 0 to 10). Query about the knee for those in total knee replacement group and hip for those in total hip replacement group.

Transfer FIM (*all time points*)

The Transfer FIM assesses the ability for the patient to either 1) transfer from a supine position in bed to standing and back **or** 2) transfer from a supine position in bed to a chair/wheelchair and back (if patient not able to safely transition to standing). With efficiency in mind, the therapist will begin formulating the FIM score when the patient begins to transition out of a supine position in bed but will not complete that process until standing and ambulation assessment is finished and the patient then transfers back into supine in bed.

Once all supine assessments have been completed the patient will be asked to get up from a supine position to standing or to a chair / wheelchair (as appropriate). As part of the VA SOC, the component parts of the transfer will be assessed and documented, as well, including a) supine to sit and b) sit to stand or sit (bed) to chair / wheelchair.

After all standing and ambulation activity (or chair activity) has been completed, the patient will be asked to get back into bed and to lie supine. Again the component parts of the transfer will be assessed and documented including a) stand to sit or chair to bed and b) sit to supine. At this point the overall FIM Transfer score can be determined.

The overall Transfer FIM and component transfers are graded on a seven point scale as follows

- 7 - Complete Independence
- 6 - Modified Independence
- 5 - Supervision / Set-up
- 4 - Minimal or Contact Assistance
- 3 - Moderate Assistance
- 2 - Maximal Assistance
- 1 - Total Assistance
- 0 - Activity did not occur due to safety or medical limitations or patient refusal

Reference the FIM Clinical Guide or other appropriate reference source if further assistance is needed in determining the 7 point score.

Note: Although not necessarily a component part of the Transfer FIM assessment, the VA SOC includes assessing and documenting Bed Mobility, as well.

Locomotion FIM (*all time points*)

It is assumed that walking will be the primary mode of locomotion upon D/C, so this FIM Locomotion score will be based on walking. After or as a continuation of the of the Self Selected Gait Speed Test, the patient will be asked to ambulate as far as they can reasonably and safely. The distance and level of assistance will be used to determine the Locomotion FIM score as follows:

- 7 - Complete Independence: Able to walk at least 150' without any assistance or device
- 6 - Modified Independence : At least 150' with assistive device or increased time
- 5 - Supervision / Set-up : At least 150' requiring Supervision / Set-up OR 50' independently
- 4 - Minimal or Contact Assistance : At least 150' and minimal assistance
- 3 - Moderate Assistance : At least 150' and moderate assistance
- 2 - Maximal Assistance : 50 -149' and assist from one person
- 1 - Total Assistance : Less than 50' and/or assist from two persons
- 0 - Activity did not occur due to safety or medical limitations or patient refusal

Reference the FIM Clinical Guide or other appropriate reference source if further assistance is needed in determining the Locomotion 7 point score.

Stair FIM (*all time points*)

If deemed to be safe and appropriate, the patient will be asked to ascend / descend 12 steps* – either a continuous flight or multiple repetitions of gym based steps. Actual attempts at stair climbing will probably not be done until at least Post-op Day 2.

- 7 - Complete Independence: Able negotiate at least 12 steps without any assistance or device
- 6 - Modified Independence : At least 12 steps with device and/or handrail and no helper
- 5 - Supervision: At least 12 steps requiring Supervision OR 4 steps with modified independence
- 4 - Minimal or Contact Assistance : At least 12 steps requiring minimal / contact assistance
- 3 - Moderate Assistance : At least 12 steps requiring moderate assistance
- 2 - Maximal Assistance : 4-11 steps and assist from one person
- 1 - Total Assistance : Less than 4 steps and/or assist from two persons
- 0 - Activity did not occur due to safety or medical limitations or patient refusal

Reference the FIM Clinical Guide or other appropriate reference source if further assistance is needed in determining the Stairs 7 point score.

* In the event that the available stairs have only 10 or 11 steps per flight, an experienced therapist will evaluate the patient's performance on the 10 or 11 steps and extrapolate their ability to do 12 steps when scoring the Stair FIM for this study.

Repeated Chair Stand Test (*baseline, post-op day 2 thru acute DC, and 6 weeks*)

This test represents the time it takes for an individual to stand from a chair 5 times with arms crossed over the chest. Participant starts sitting in a chair. Start to time when participant starts to stand the first time and stop when participant reaches a full upright position on the 5th chair stand.

The tester stands close to the side of the chair for safety and to observe the test to ensure the participant comes to a full stand and full sit position during the test. A practice trial is recommended before testing to check whether the participant is able to stand up and to check understanding of the test.

Tester Script:

“The next test measures the strength in your legs. Do you think it would be safe for you to try to stand up from a chair without using your arms?” (Demonstrate and explain the procedure.) ***“First, fold your arms across your chest and sit so that your feet are on the floor; then stand up keeping your arms folded across your chest.”*** If it is unsafe to attempt the chair stand or the participant cannot rise without using arms this is the end of the test. Record result (i.e., test was not attempted). If participant is able to stand, continue: ***“Now that you attempted once, please stand up straight as QUICKLY as you can five times, without stopping in between. After standing up each time, sit down and then stand up again. Keep your arms folded across your chest. I’ll be timing you with a stopwatch.”*** When the participant is properly seated, say: ***“Ready? Stand”*** and begin timing. Count out loud as the participant arises each time, up to five times. Stop the stopwatch when he/she has straightened up completely for the fifth time. Additionally, stop the test if:

- Participant becomes tired or short of breath during repeated chair stands or at your discretion, if concerned for participant’s safety
- Participant uses his/her arms
- After 1 minute, if participant has not completed rises.

If the participant stops and appears to be fatigued before completing the five stands, confirm this by asking “Can you continue?” If participant says “Yes,” continue timing. If participant says “No,” stop the test.

Stair Climbing Test (*baseline and 6 weeks*) - This is a test of ascending stairs. It records the time in seconds it takes to ascend a 10 step flight of stairs.

- Equipment: timer/stop watch and flight of stairs. Steps heights should be standard (between 16-20cm), and the location of the stairs should have adequate lighting and free from traffic and external distractions.
- Tester: if safety is a concern the test should not be done. The tester can guard behind/below the participant going up the stairs or stay in the starting platform (Allow participant to climb a couple of steps before testing to assess for safety). The use of a handrail is mandatory. The use of walking aid is permitted.
- Scoring: timing starts in the signal to begin and terminates when the participant finishes ascending the steps (time is recorded). The participant can stop and rest during the test if needed but the time keeps on going.

Tester Script

“You will ascend the flight of stairs as quickly as possible but in a safe manner. Start with both feet on the bottom landing. On begin, go to the top of the stairs as fast but as safe as you can. Always use the handrail. Ready, begin”

The following information is provided in the event that varying step number and dimensions dictates calculation of power to make like comparisons.

1. On 9W (main hospital building), each flight of stairs has 10 steps. The height of each step is 17.5 cm and the depth is 27 cm.
2. On 5W (main hospital building) by the “stepdown unit”- each flight of stairs has 10 steps. The height of each step is 17.5 cm and the depth is 27.7 cm.
3. In the ROB, there are 15 steps per flight and the height of each step is 17 cm and the depth is 26 cm. When testing in ROB, time taken to ascend upper 10 steps of flight will be recorded.

Single Leg Stance (SLS) (*baseline and 6 weeks*). The SLS is recommended in a battery of tests to quickly assess global functional level and its scores are related to risk for falls.

- Participants are asked to stand on one foot for 45 seconds. The other foot is raised so that the raised foot is near but not touching the ankle of their stance limb.
- The participant may use the arms, bend the knee, or move the body to maintain balance.
- The tester uses a stopwatch to measure the amount of time the participant is able to stand on one limb. Time commences when the participant raises the foot off the floor. Time ends when the participant either: (1) uses the raised foot (moved it toward or away from the standing limb or touched the floor), (2) moves the weight-bearing foot to maintain his balance (ie, rotated foot on the ground), (3) a maximum of 45 seconds elapses. Three trials are performed in each side and recorded.

Tester Script:

Now I will show you the test. (Demonstrate) I want you to try to stand on one foot with the other foot raised near, but not touching the ankle, for about 45 seconds. You may use your arms, bend your knees, or move your body to maintain your balance, but try not to move your feet. Try to hold this position until I tell you to stop. We will do it three times.

Stand next to the participant to help him/her into the tandem position. Supply just enough support to the participant's arm to prevent loss of balance. When the participant has raised his/her foot, ask “Are you ready?” Then let go and begin timing as you say, “Ready, begin.” Stop the stopwatch and say “Stop” after 45 sec. or when the participant steps out of position or grabs your arm or steady surface.

Pain Intensity (*all time points*) - At the end of each testing session ask the participant to rate the current level of pain (from 0 to 10) in the knee (for those in total knee replacement group) or hip (for those in total hip replacement group) at that time and record it.

PROCEDURE AND LOGISTICS SECTION (Please refer to attached work flow chart)

Weekdays: VA hospital PT's will complete morning PT assessments and interventions including Initial Evaluations for Day 1 post-op patients. Assessment data will be documented on paper CEX form. University of Pittsburgh PT's will complete PT assessments, FALLS-IH form, and interventions during afternoon sessions. University of Pittsburgh PT's will enter all data from paper copies into REDCap including data collected from morning and afternoon sessions; data entry status will be updated to "Unverified" once PT data entry for event is complete.

Saturday: University of Pittsburgh PT's will complete questionnaires on Saturday morning prior to any physical therapy. University of Pittsburgh PT's will perform morning assessments and interventions. University of Pittsburgh PT's will complete PT Initial Evaluation on Saturday for Post-Op Day 1 patients during morning session, input the initial evaluation into the VA CPRS documentation system, sign completed evaluation, and collect all research related data. During completion of PT Initial Evaluation, discharge recommendations must be completed. An email will be sent to VA PT Coordinator for any Durable Medical Equipment dispensed including wheeled walker, cane, or wheelchair. University of Pittsburgh PT's will enter data from paper copies into REDCap for data collected from morning sessions; data entry status will be updated to "Unverified" once PT data entry for event is complete. VA Rehab Staff will complete afternoon sessions on Saturday including assessment, CEX forms, and interventions.

Sunday: University of Pittsburgh PT's will complete questionnaires on Sunday morning prior to any physical therapy. University of Pittsburgh PT's will perform morning assessments and interventions. University of Pittsburgh PT's will enter data from paper copies into REDCap; data entry status will be updated to "Unverified" once PT data entry for event is complete. VA Rehab Staff will complete afternoon sessions on Sunday including assessment, CEX forms, and interventions.

****Any missing PT assessment data will be communicated with VA Rehab Supervisor on a daily basis.**

****Any Adverse Events, Serious Adverse Events, or Protocol deviations should be communicated to the Study Coordinator within IRB guidelines.**

Document Management:

Study Coordinator will place CEX forms and FALLS forms for each study participant in locked file storage in PT office space at 2W113. VA and Pitt PTs will retrieve appropriate forms prior to participant assessment / intervention and / or REDCap data entry and return to file storage in 2W113 once completed. Study Coordinator will retrieve completed forms daily (weekdays) and archive elsewhere.

PT Related Locations:

Baseline Evaluations/ 6-Week Follow-ups: Completed preferably in the Research Office Building and will be completed by University of Pittsburgh PT's.

Post- Op Day 1: Completed in Patient Room on Floors 4,5,6 in Building 1

Post-op Day 2 thru Acute DC: PT gym 2nd Floor or Patient Room Floors 4,5,6 Building 1

Discharge Day: PT gym 2nd Floor or Patient Room Floors 4,5,6 Building 1

Nerve Block Study – Physical Therapy Clinical Examination MOP – Rev. 06/14/2016

Day	Location	Task	Responsibility	
Baseline	Research Building (pref) OR IMPAC Clinic 9W (alt)	Determine eligibility & obtain consents	Research Coordinator	
		Perform baseline assessment and enter data into REDCap	Pitt PTs	
Day of Surgery	Same Day Surgery Area (pre-surgery) / Pt. Room (post)	Administer Appropriate Surveys Pre & Post Surgery	Research Coordinator	
Joint Replacements at VA are usually performed on Mondays & Fridays				
Post-op Day 1 to Day n	Pt. Room Floors 4,5,6 (Typically 5W-MED) Building 1 OR PT Gym Areas on 2 nd Floor	Administer Pt. Surveys (AM, pre PT)	Monday to Friday – Research Coordinator	
			Saturday & Sunday – Pitt PTs	
		Complete FALLS IH Form	PM Monday to Friday – Pitt PTs	
			AM Saturday & Sunday – Pitt PTs	
		Perform VA SOC Evaluation Post-op day 1	Sunday to Friday – VA PTs	
			Saturday – Pitt PTs	
		Perform PT Acute Study Assessment On 2nd Post-op day, add Repeated Chair Stand Test to PT Acute Study Assessment until Acute DC.	AM Monday to Friday – VA PTs	
			PM Monday to Friday – Pitt PTs	
			AM Saturday & Sunday – Pitt PTs	
			PM Saturday & Sunday – VA Rehab Staff / PTs	
			Review / progress exercises	AM Monday to Friday – VA PTs
				PM Monday to Friday – Pitt PTs
				AM Saturday & Sunday – Pitt PTs
				PM Saturday – VA OT
		PM Sunday – VA PTs		
		Enter Assessment Data to REDCap	Pitt PTs	
6 week Follow-up	Research Building (pref) OR IMPACT Clinic 9W (alt)	Perform 6 week Follow-up Study Assessment and enter data into REDCap	Pitt PTs	

** Pitt PTs will provide back-up for Study Coordinator for consenting and administering surveys as needed.

Appendix A – VA Hospital Codes

CONDITION A: Cardiac or respiratory arrest, or when victim is unresponsive.

CONDITION C: Any other life threatening condition where the victim needs rapid evaluation and/or treatment.

{Personnel unsure of the nature or severity of the emergency should initiate a Condition A.}

CODE BLUE: Behavioral emergencies including aggressive, assaultive, disruptive or violent behavior

CODE ORANGE: Fire Emergency

CODE SILVER: Active threat (person using a weapon) on VA property.

CODE HELP: Medical concerns perceived by the Veteran/significant others as follows: there is an emergency situation and you are unable to get the attention of hospital staff, there is a noticeable medical change in the Veteran's condition and the health care team is not recognizing the concern, or if there is a situation where you have spoken to the hospital staff and manager and you continue to have serious concerns regarding how care is being provided, managed, or planned.

CODE ADAM: VA Police will make a CODE ADAM ALERT announcement on the overhead paging system at facility where child was reported missing. The announcement will also include a description of child and all other pertinent information to aide all medical staff in the search.

****To activate any of these codes, you will dial 911 from any hardwired telephone; tell the operator the condition; then give the facility, building, floor and room number; afterwards, make sure to listen to the overhead message to ensure the proper area and code is announced.

Appendix B – Access Information

Access Codes	
Location	Code
Stairwells – 5 th Floor West	1234*
Rm 5W143 – Supplies including oxygen tanks	1357*
Rm 5W142 – Linens	1313*



Date _____

Dear _____,

As per our recent discussion, you are being invited to take part in a research study that has been funded by the Department of Defense because you are scheduled to have either a Total Hip Replacement (THA) or a Total Knee Replacement (TKA). Before you decide to take part, it is important that you know why the research is being done and what it will involve. Enclosed is the Informed Consent Form for the **4-Drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty Analgesia in Veterans (Nerve Block Study)**. Please review the Consent completely, review it with your family/friends if you wish and note any questions that you may have.

On _____, either I, or another member of the study team, will call you to ask if you are interested in participating in the study and answer any questions you may have. Feel free to ask us about anything that is unclear to you or if you would like more detail. Should you decide to participate, also during this call, we will set up an appointment for you to come to the VA Pittsburgh-University Drive location to sign consent and complete the Screening and Baseline Study Visits.

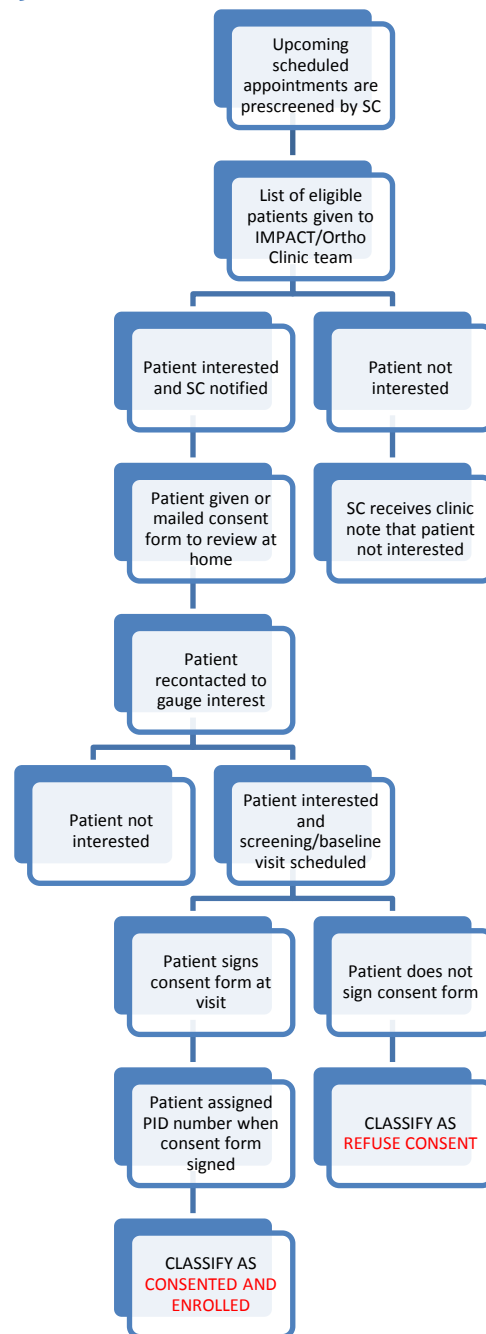
Thank you for taking the time to talk with me.

Best regards,

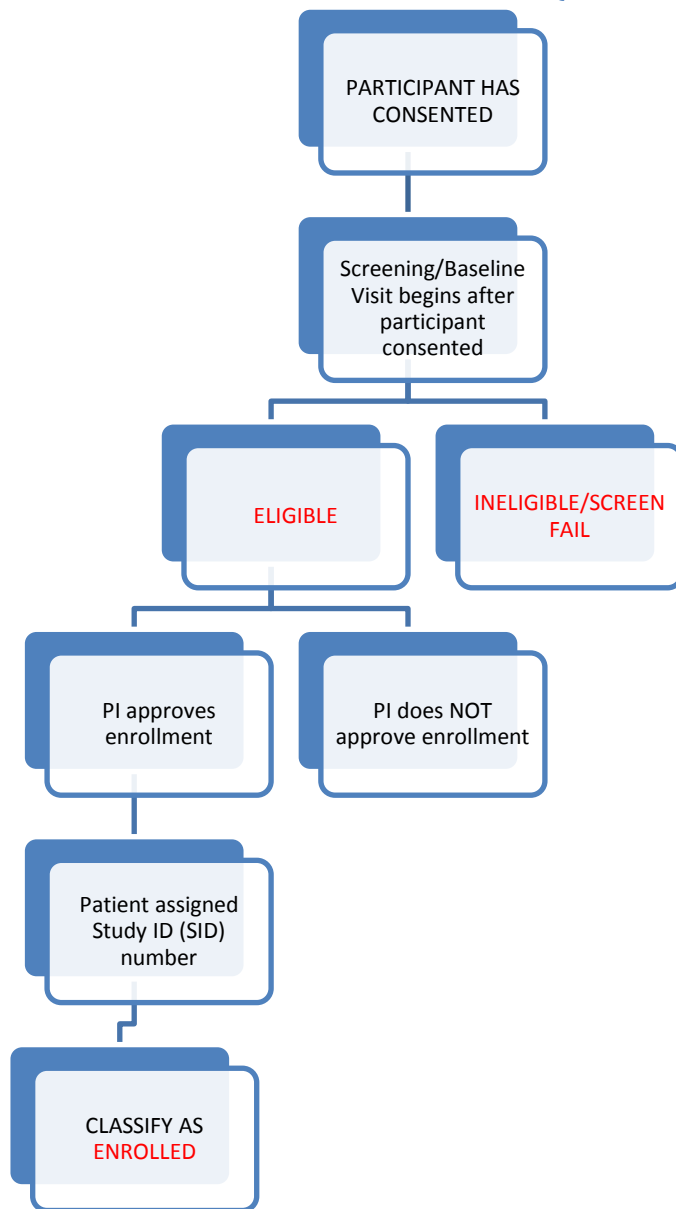
Staff Member Name

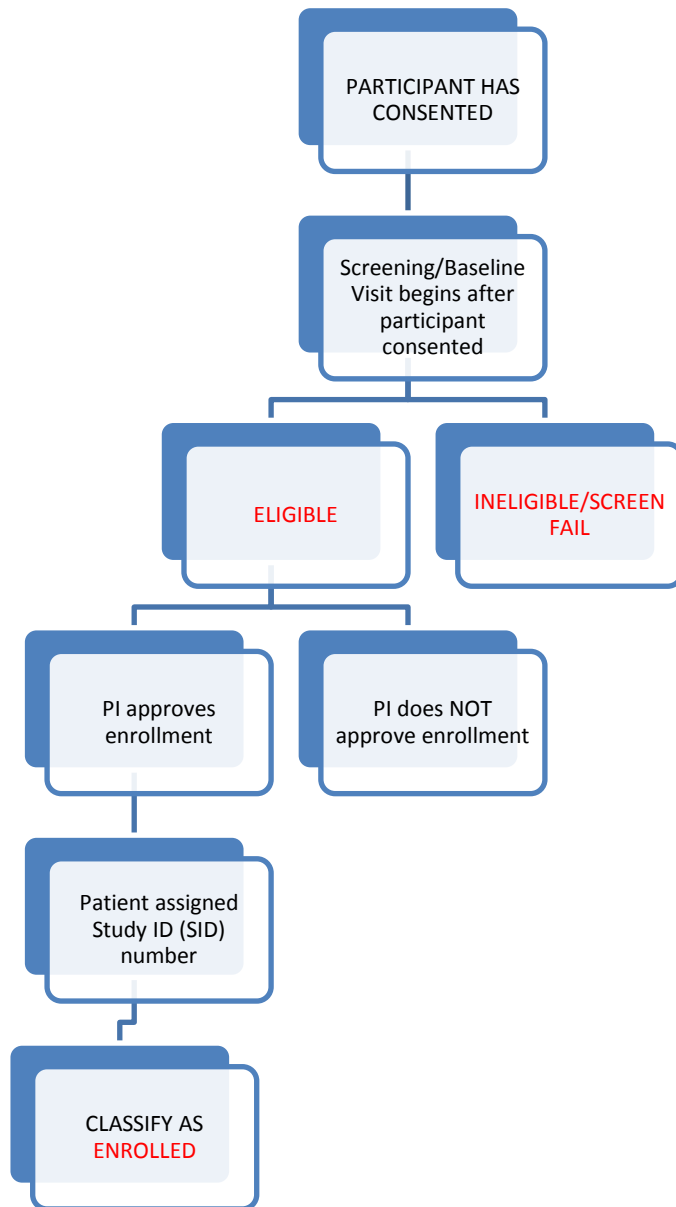
Staff Member Telephone #

PROCESS FLOWCHART: FROM PRESCREENING TO OBTAINING INFORMED CONSENT (Screening/Baseline Visit)

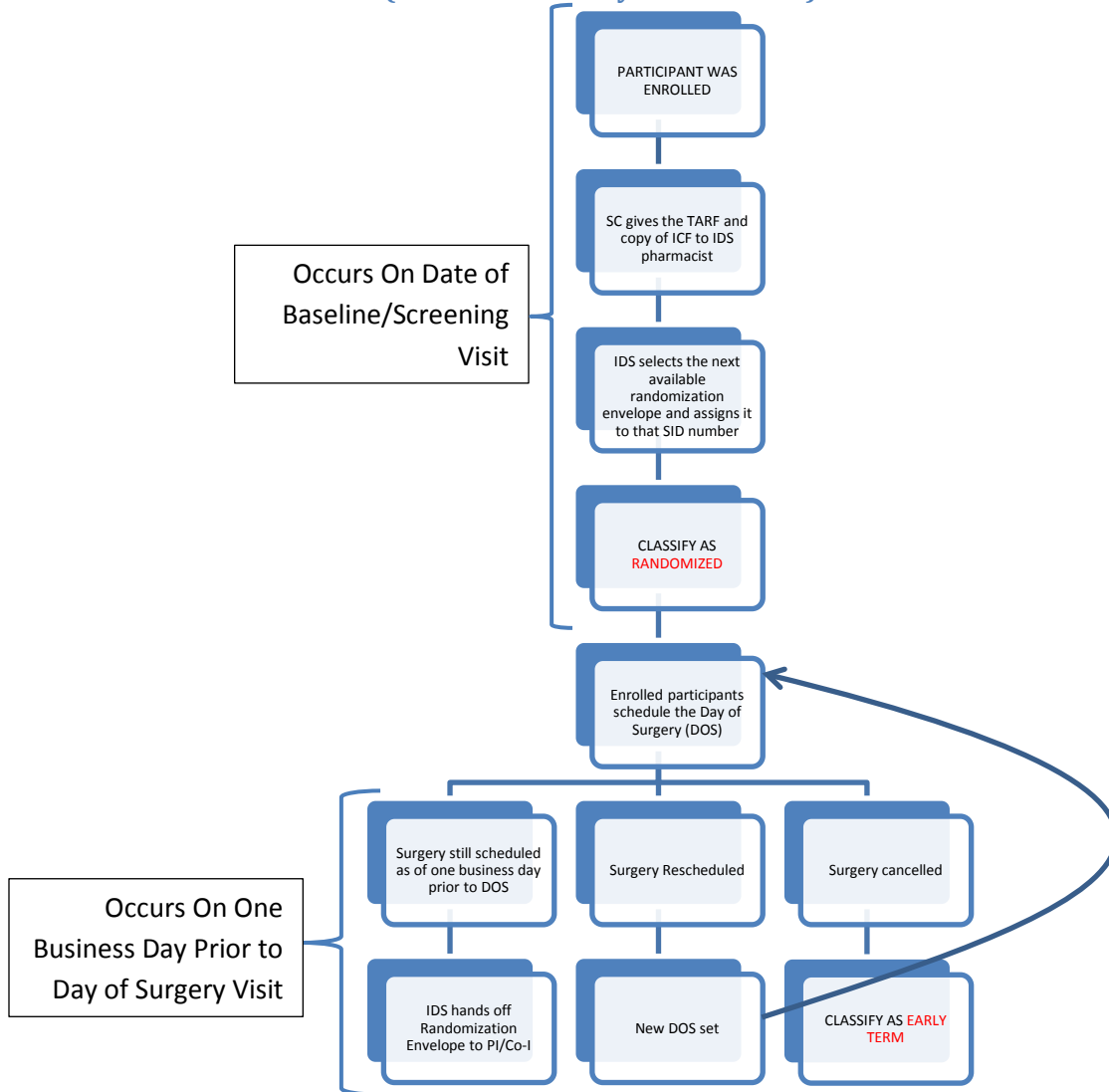


PROCESS FLOWCHART: FROM CONSENTED TO ENROLLED (Screening/Baseline Visit)

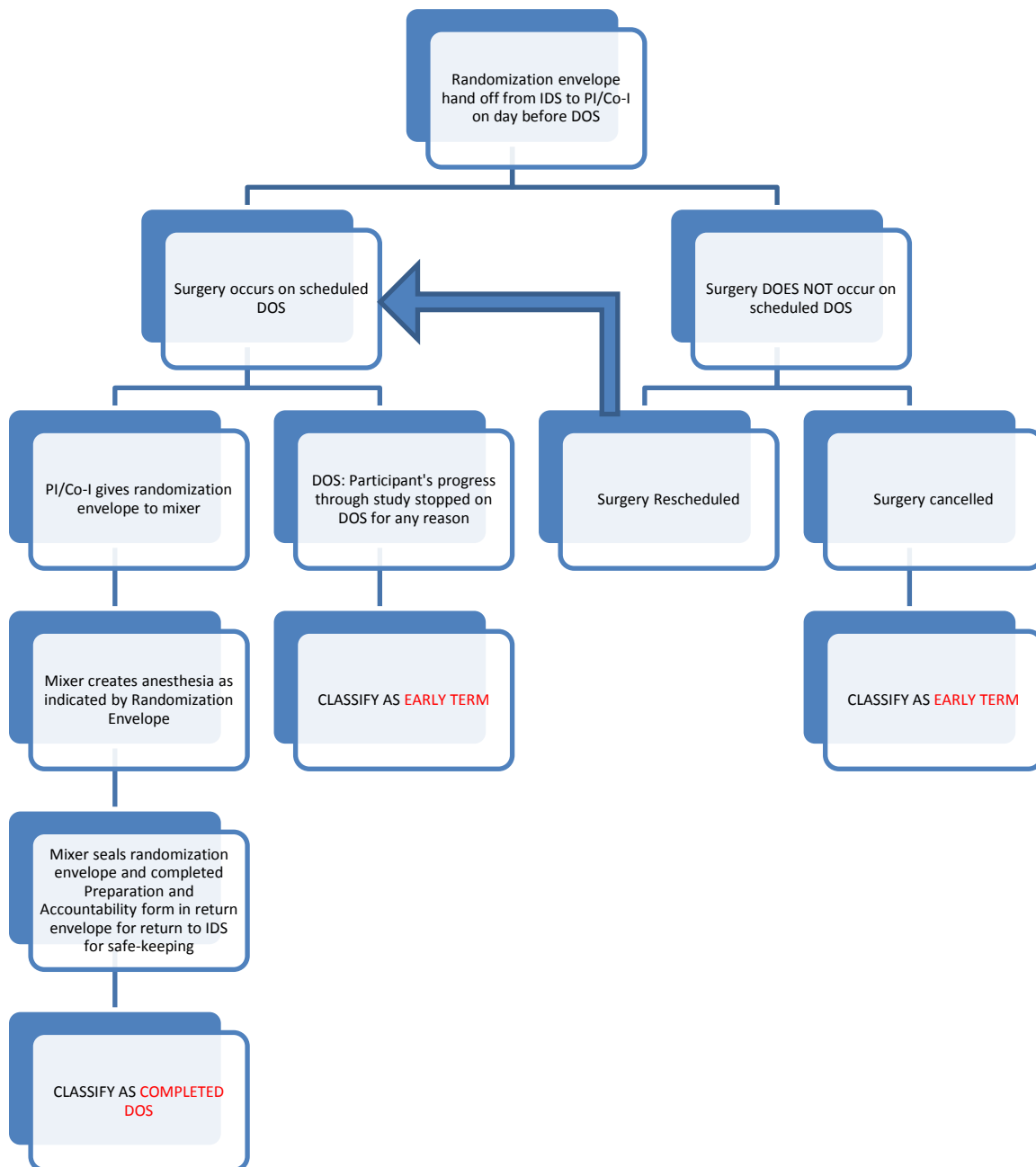




PROCESS FLOWCHART: FROM ENROLLED (Screening/Baseline Visit) TO RANDOMIZATION ENVELOPE HANDOFF (One Business Day Prior to DOS)



PROCESS FLOWCHART: FROM RANDOMIZATION ENVELOPE HANDOFF (One business day prior to DOS) TO ANESTHESIA PREPARATION (DOS)



WHO/WHAT/WHERE/WHEN

Each patient “Visit” requires the completion of a research note in CPRS. Following is a brief description of the who’s, what’s and where’s of these notes.

SCREENING VISIT:

- Research Initial Consent Note (Clinic: **PIT-UE-SURGRESEARCH-BW-X**)
- Research Study Alert (Clinic: **PIT-UE-SURGRESEARCH-BW-X**)

BASELINE VISIT:

- Research Note – Questionnaires (Clinic: **PIT-UE-SURGRESEARCH-BW-X**)
- Research Note – PT (Clinic: **PIT-UE-PTRESEARCH-VK-X**)

ALL OTHER STUDY VISITS:

- Research Note – Questionnaires (Clinic: **PIT-UE-SURGRESEARCH-BW-X**)
- Physical Therapy *Consult* – Research: (Clinic: **PIT-UE-PTRESEARCH-VK-X**)
- Physical Therapy – Research: (Clinic: **PIT-UE-PTRESEARCH-VK-X**)

If the Screening and Baseline Visits are performed on the same day, a Research Initial Consent Note, Research Study Alert and Research Note must all be completed.

HOW

1. Sign into CPRS
2. Select patient by entering initial and last 4 digits of the SSN (M****) or the patient's name (Last Name First eg.: ZZMouse,Minnie – NO SPACES)
 - a. If more than one patient has the same initial and last 4, double-click on the correct patient
3. Across the top of the Cover Sheet page, click on “Visit Not Selected – Current Provider Not Selected”

The screenshot shows the VISTA CPRS interface for patient ZZMOUSE, MINNIE (OUTPATIENT). The top navigation bar includes buttons for 'Visit Not Selected' and 'Current Provider Not Selected'. A green arrow points to the 'Visit Not Selected' button, with the text 'Step 3' next to it. The main content area displays various patient information sections:

- Active Problems:** Dementia Nos (ICD-9-CM 294.0), Dementia With Long Episodes (ICD-9-CM 331.82), Capd (ICD-9-CM 495.1), Right Mastoiditis (ICD-9-CM 798.9), Hypertension, Essential (ICD-9-CM 401.9), Carpal Tunnel Syndrome (ICD-9-CM 354.0).
- Allergies / Adverse Reactions:** Cheddar Cheese, Cat Dander, Walnut, Vancomycin, Penicillin, Nonsteroidal Anti-Inflammatory, Cephalosporin, Sulfonamides, Metoprolol (Lopressor), Morphine, Docosate (Colace), Furosemide (Lasix).
- Active Medications:** Non-Va Zosyn 800mg Tab, Active; Non-Va Maxipride Hcl 50mg Tab, Active; Non-Va A & D Oint, Active; Non-Va Multivitamin Cap/Tab, Active; Non-Va Omeprazole 20mg Ec Cap, Active; Non-Va Belladonna Alk 0.13/Phenothiaz 16mg/5ml, Active; Non-Va Kava Cap/Tab, Active; Non-Va Belladonna Alk 0.13/Phenothiaz 16mg/5ml, Active; Non-Va St John's Wort Cap/Tab, Active; Non-Va Anacin Cap/Tab, Active; Non-Va Garlic Oil Cap/Tab, Active; Non-Va No Reported Non-Va Med Use By Patient, Active; Non-Va A & D Oint, Active; Non-Va Melatonin 3mg Cap/Tab, Active; Non-Va Melatonin 3mg Cap/Tab, Active.
- Clinical Reminders:** Adv Dis Psych (BH Nurse/Provider), DUE NOW; Alcohol Screen (Nurse/Provider), Sep 16,15; Tobacco Use Screen (Nurse/Provider), Mar 30,09; Depression Screen (Nurse/Provider), DUE NOW; Education/Communication (Nurse), Jul 30,14; Evaluation of + Depression Screen, DUE NOW; Hep C Risk Screen (Nurse/Prov), DUE NOW; Mod Reconciliation (Provider), Jul 09,15; Pain Assessment Outpt (Nurse), Jul 14,15; Pressure Ulcer Prevention (Nurse), DUE NOW; Pressure Ulcer Prevention (Prov), DUE NOW; PTSD Screen (Nurse/Provider), Nov 07,14; Evaluation of + PTSD Screen, DUE NOW; Suicide Screen (BH Provider), Dec 10,08; Abuse/Neglect Screen (Nurse/Prov), DUE NOW; Tetanus Toxoid Due (Nurse/Provider), DUE NOW; Homelessness Screening (Nurse/Prov), DUE NOW; My Health/Well Interest (Nurse/Prov), DUE NOW; Pneum13 (Nurse/Prov) Pneumococcal, DUE NOW; Return to Clinic (Provider), DUE NOW.
- Recent Lab Results:** No Orders Found.
- Vitals:** T Refused Jan 28,2016 14:47; P 39 Jan 28,2016 14:43; R 28 Jan 28,2016 14:47; BP 88/50 Jan 28,2016 14:47; HT 53 in Jan 28,2016 10:00(134.62 cm); WT 43 lb Jan 28,2016 10:00(19.50 kg); PN 9 Mar 17,2016 10:45; nov oo Jan 28,2016 14:47. Lying femoral left at rest. ACTUAL STANDING WEIGHT.
- Appointments/Visits/Admissions:** No data found.

The bottom of the screen shows a taskbar with various application icons and a system clock indicating 2:48 PM on 8/19/2016.

4. Provider & Location for Current Activities Box will open
5. In the Encounter Provider section, enter your name

Vista CPRS in use by: Gilbert, Karen L. (vista.pittsburgh.med.va.gov)

File Edit View Tools Help

ZZMOUSE, MINNIE (OUTPATIENT) Visit Not Selected No PACT assigned at any VA location /

000-00-9191 Jan 01, 1910 (106) Current Provider Not Selected

Flag VistalWeb Postings
Remote Data WAD

Active Problems

- Dementia Nos (ICD-9-CM 294.8)
- Dementia With Lewy Bodies (ICD-9-CM 331.82)
- Copd (ICD-9-CM 486)
- Right Mass Chest (ICD-9-CM 799.9)
- Hypertension, Essential (ICD-9-CM 401.9)
- Carpal Tunnel Syndrome (ICD-9-CM 354.0)

Allergies / Adverse Reactions

- Cheeddar Cheese
- Cat Dander
- Warfarin
- Vancomycin
- Peanuts
- Nonsteroidal Anti-Inflammatory
- Cephalexin
- Sulfonamides
- Metoprolol (Lopressor)
- Morphine
- Docusate (Colace)
- Furosemide (Lasix)

Postings

- Research Study Alert - Warning
- Smoking Risk - Warning Aug 20, 2008
- Suicide Risk - Warning Dec 10, 2007
- Elopement Risk - Warning
- Advance Directive Nov 24, 2015

Active Medications

- Non-Va Zorprin 800mg Tab Active
- Non-Va Moprolol 50mg Tab Active
- Non-Va A & D Oint Active
- Non-Va Multivitamin Cap/Tab Active
- Non-Va Omeprazole 20mg Ec Cap Active
- Non-Va Belladonna Alk 0.13/Phenobarb 16mg/5ml Active
- Non-Va Kava Cap/Tab Active
- Non-Va Belladonna Alk 0.13/Phenobarb 16mg/5ml Active
- Non-Va St John's Wort Cap/Tab Active
- Non-Va Anasch Cap/Tab Active
- Non-Va Garlic Oil Cap/Dial Active
- Non-Va No Reported Non-Va Med Use By Patient Active
- Non-Va A & D Oint Active
- Non-Va Melatonin 3mg Cap/Tab Active
- Non-Va Melatonin 3mg Cap/Tab Active

Clinical Reminders

- Adv Dir/Phys (BH Nurse/Provider) DUE NOW
- Alcohol Screen (Nurse/Provider) Sep 16, 15
- Tobacco Use Screen (Nurse/Provider) Mar 30, 09
- Depression Screen (Nurse/Provider) DUE NOW
- Education/Communication (Nurse) Jul 30, 14
- Evaluation of + Depression Screen DUE NOW
- Hep C Risk Screen (Nurse/Prov) DUE NOW
- Med Reconciliation (Provider) Jul 09, 15
- Pain Assessment Outpt (Nurse) Jul 14, 15
- Pressure Ulcer Prevention (Nurse) DUE NOW
- Pressure Ulcer Prevention (Prov) DUE NOW
- PTSD Screen (Nurse/Provider) Nov 07, 14
- Evaluation of + PTSD Screen DUE NOW
- Suicide Screen (BH Provider) Dec 10, 08
- Abuse/Neglect Screen (Nurse/Prov) DUE NOW
- Tetanus Toxoid Due (Nurse/Provider) DUE NOW
- Homelessness Screening (Nurse/Prov) DUE NOW
- My Health/Interest (Nurse/Prov) DUE NOW
- Pneum13 (Nurse/Prov) Pneumococcal DUE NOW
- Return to Clinic (Provider) DUE NOW

Provider & Location for Current Activities

Encounter Provider

- Abay, Rebecca - MEDICAL STUDENT
- Abbott, Paul H - PHYSICIAN ASSISTANT
- Abdalla, Hossam Elmad - RENAL FELLOW
- Abdel, Emman S - ATTENDING PHYSICIAN
- Abdel, Catherine P - TECHNICIAN
- Abel, Jennifer C - CONTRACTOR
- Abraham, Neelhu - INTERN

Encounter Location

< Select a location from the tabs below... >

Clinic Appointments Hospital Admissions New Visit

Visit Location

- BWORM
- A KIOSK TEST
- A-CDM MED PRO FEES
- A-INPT DIAGNOSTIC PRO FEE
- A-INPT MED PRO FEES
- A-INPT RADIOLOGY PRO FEES
- A-UNAUTHORIZED FEE (NC)X

Date/Time of Visit

NOW

☐ Historical Visit: a visit that occurred at some time in the past or at some other location (possibly non-VA) but is not used for workload credit.

Recent Lab Results

No Orders Found

Vitals

Parameter	Value	Date/Time
T	Refused	Jan 28, 2016 14:47
P	39	Jan 28, 2016 14:43
R	28	Jan 28, 2016 14:47
BP	88/50	Jan 28, 2016 14:47
HT	53 in	Jan 28, 2016 10:00 (134.62 cm)
WT	43 lb	Jan 28, 2016 10:00 (19.50 kg)
PN	8	Mar 17, 2016 10:46

ACTUAL STANDING WEIGHT

Appointments/Visits/Admissions

No data found

Cover Sheet Problems Meds Orders Notes Consults Surgery D/C Summ Labs Reports

Windows Taskbar: 2:52 PM 8/19/2016

6. Highlight
7. In the Encounter Location section, click on New Visit tab. In the Visit Location section:
 - a. If entering a Research Alert, Research Initial Consent Note or a questionnaire-centric patient visit, the location is **PIT-UE-SURGRESEARCH-BW-X**
 - b. If entering *any* PT Visit, the location is **PIT-UE-PTRESEARCH-VK-X**
8. Do NOT click on the box that refers to a Historical Visit.
9. Click OK or Enter

VISTA CPRS in use by: Gilbert, Karen L. (vista.pittsburgh.med.va.gov)

File Edit View Tools Help

ZZMOUSE, MINNIE (OUTPATIENT) Visit Not Selected No PACT assigned at any VA location /
000-00-9131 Jan 01, 1910 (106) Current Provider Not Selected

Active Problems: Dementia Nos (ICD-9-CM 294.8), Dementia With Lewy Bodies (ICD-9-CM 331.82), Copd (ICD-9-CM 496), Right Mass Chest (ICD-9-CM 793.9), Hypertension, Essential (ICD-9-CM 401.9), Carpal Tunnel Syndrome (ICD-9-CM 354.0)

Allergies / Adverse Reactions: Cheddar Cheese, Cat Dander, Warfarin, Vancomycin, Penicillin, Nonsteroidal Anti-Inflammatory, Cephalosporin, Sulfonamides, Metoprolol (Lopressor), Morphine, Docosate (Colace), Furosemide (Lasix)

Active Medications: Non-Va Zosyn 800mg Tab, Active; Non-Va Magnesium Hydroxide 500mg Tab, Active; Non-Va A & D Oint, Active; Non-Va Multivitamin Cap/Tab, Active; Non-Va Omega-3 20mg Ec Cap, Active; Non-Va Belladonna Alk 0.13/Phenobarb 15mg/5ml, Active; Non-Va Kava Cap/Tab, Active; Non-Va Belladonna Alk 0.13/Phenobarb 15mg/5ml, Active; Non-Va Ativan Cap/Tab, Active; Non-Va Garlic Oil Cap/Dial, Active; Non-Va No Reported Non-Va Med Use By Patient, Active; Non-Va A & D Oint, Active; Non-Va Melatonin 3mg Cap/Tab, Active; Non-Va Melatonin 3mg Cap/Tab, Active

Clinical Reminders: Adv Dis/Psych (BH Nurse/Provider) DUE NOW/ Sep 16, 15; Alcohol Screen (Nurse/Provider) Mar 30, 09; Tobacco Use Screen (Nurse/Provider) DUE NOW/ Jul 30, 14; Depression Screen (Nurse/Provider) DUE NOW/ Jul 30, 14; Education/Communication (Nurse) DUE NOW/ Jul 30, 14; Evaluation of + Depression Screen DUE NOW/ Jul 30, 14; Hep C Risk Screen (Nurse/Prov) DUE NOW/ Jul 08, 15; Med Reconciliation (Provider) Jul 14, 15; Pain Assessment Outpt (Nurse) DUE NOW/ Nov 07, 14; Pressure Ulcer Prevention (Nurse) DUE NOW/ Nov 07, 14; Pressure Ulcer Prevention (Prov) DUE NOW/ Nov 07, 14; PTSD Screen (Nurse/Provider) DUE NOW/ Dec 10, 08; Evaluation of + PTSD Screen DUE NOW/ Dec 10, 08; Suicide Screen (BH Provider) DUE NOW/ Dec 10, 08; Abuse/Neglect Screen (Nurse/Prov) DUE NOW/ Dec 10, 08; Tetanus Toxoid Due (Nurse/Provider) DUE NOW/ Dec 10, 08; Hunger/Starvation Screening (Nurse/Prov) DUE NOW/ Dec 10, 08; My Health/Interest (Nurse/Prov) DUE NOW/ Dec 10, 08; Pneum13 (Nurse/Prov) Pneumococcal Return In Clinic (Provider) DUE NOW/ Dec 10, 08

Postings: Allergies, Research Study Alert - Warning, Smoking Risk - Warning Aug 20, 2008, Suicide Risk - Warning Dec 10, 2007, Firearm Risk - Warning, Advance Directive Nov 24, 2015

Provider & Location for Current Activities

Encounter Provider: Gilbert, Karen L - CLINICAL RESEARCH COORDINATOR

Encounter Location: PIT-UE-SURGRESEARCH-BW-X Aug 19, 16 14:59

Visit Location: PIT-UE-SURGRESEARCH-BW-X

Date/Time of Visit: NOW

Historical Visit: ☐ Historical Visit - a visit that occurred at some time in the past or at some other location (possibly non-VA) but is not used for workload credit

Recent Lab Results: No Orders Found

Vitals: T 98.6, P 33, R 28, BP 88/50, HT 53 in, WT 43 lb, PN 8, Jan 28, 2016 14:47, LYING FEMORAL LEFT AT REST, ACTUAL STANDING WEIGHT

Appointments/Visits/Admissions: No data found

Cover Sheet Problems Alerts Orders Notes Consults Surgery D/C Summ I obs Reports

Vista CPRS in use by: Gilbert, Karen L. (vista.pittsburgh.med.va.gov)

File Edit View Tools Help

ZZMOUSE, MINNIE (OUTPATIENT) Visit Not Selected No PACT assigned at any VA location /

000-00-9131 Jan 01, 1910 (108) Current Provider Not Selected

Visit/Web Remote Data Postings WAD

Active Problems

- Dementia Nos (ICD-9-CM 294.8)
- Dementia With Lewy Bodies (ICD-9-CM 331.82)
- Copd (ICD-9-CM 496.)
- Right Mass Chest (ICD-9-CM 799.9)
- Hypertension, Essential (ICD-9-CM 401.9)
- Capal Tunnel Syndrome (ICD-9-CM 354.0)

Allergies / Adverse Reactions

- Cheddar Cheese
- Cal Diander
- Warfarin
- Vancocycin
- Peanuts
- Nonsteroidal Anti-Inflammatory
- Cephalexin
- Sulfu Drugs
- Metoprolol (Lopressor)
- Morphine
- Docusate (Colace)
- Furosemide (Lasix)

Postings

- Allergies
- Research Study Alert - Warning
- Smoking Risk - Warning Aug 20, 2008
- Suicide Risk - Warning Dec 10, 2007
- Elopement Risk - Warning
- Advance Directive Nov 24, 2015

Active Medications

Medication	Active	Due Date
Non-Va Zoprin 80mg Tab	Active	DUE NOW
Non-Va Magnoline Hol 50mg Tab	Active	Sep 16, 15
Non-Va A & D Oint	Active	Mar 30, 09
Non-Va Multivitamin Cap/Tab	Active	DUE NOW
Non-Va Omeprazole 20mg Ec Cap	Active	Jul 30, 14
Non-Va Belladonna Alk 0.13/Phenobarb 16mg/5ml	Active	DUE NOW
Non-Va Kava Cap/Tab	Active	DUE NOW
Non-Va Belladonna Alk 0.13/Phenobarb 16mg/5ml	Active	DUE NOW
Non-Va St John's Wort Cap/Tab	Active	Jul 09, 15
Non-Va Anach Cap/Tab	Active	Jul 14, 15
Non-Va Garlic Oil Cap/Oral	Active	DUE NOW
Non-Va No Reported Non-Va Med Use By Patient	Active	DUE NOW
Non-Va A & D Oint	Active	Nov 07, 14
Non-Va Melatonin 3mg Cap/Tab	Active	DUE NOW
Non-Va Melatonin 3mg Cap/Tab	Active	DUE NOW

Clinical Reminders

Reminder	Due Date
Adv Dis/Psych (BH Nurse/Provider)	DUE NOW
Alcohol Screen (Nurse/Provider)	Sep 16, 15
Tobacco Use Screen (Nurse/Provider)	Mar 30, 09
Depression Screen (Nurse/Provider)	DUE NOW
Education/Communication (Nurse)	Jul 30, 14
Evaluation of + Depression Screen	DUE NOW
Hep C Risk Screen (Nurse/Prov)	DUE NOW
Med Reconciliation (Provider)	Jul 09, 15
Pain Assessment Output (Nurse)	Jul 14, 15
Pressure Ulcer Prevention (Nurse)	DUE NOW
Pressure Ulcer Prevention (Prov)	DUE NOW
PTSD Screen (Nurse/Provider)	Nov 07, 14
Evaluation of + PTSD Screen	DUE NOW
Suicide Screen (BH Provider)	Dec 10, 08
Abuse/Neglect Screen (Nurse/Prov)	DUE NOW
Tetanus Toxoid Due (Nurse/Provider)	DUE NOW
Homelessness Screening (Nurse/Prov)	DUE NOW
My Health/et Interest (Nurse/Prov)	DUE NOW
Pnevmar13 (Nurse/Prov) Pneumococcal	DUE NOW
Return to Clinic (Provider)	DUE NOW

Provider & Location for Current Activities

Encounter Provider

- Gilbert, Karen L - CLINICAL RESEARCH COORDINATOR
- Gilbert, Clifton D - REGISTERED NURSE
- Gilbert, Karen L - CLINICAL RESEARCH COORDINATOR
- Gilbert, Sharon F - NURSING ASSISTANT, PATIENT CARE SVC
- Gilbert, Sharon M - CPAC FACILITY REVENUE TECH, CPAC MID
- Gilboa, Noam - Physician
- Gilkey, Lillie J
- Gil, Jamie L - CPAC BILLING SUPERVISOR

Encounter Location

PIT-UE-PTRESEARCH-WK-X Aug 19, 16 15:01

Clinic Appointments **Hospital Admissions** **New Visit**

Visit Location

- PIT-UE-PTRESEARCH-WK-X
- PIT-UE-PTRESEARCH-WK-X
- PIT-UE-PULMRESEARCH-IF
- PIT-UE-PULMSLEEPTLETERES-CA
- PIT-UE-RENAL RESEARCH-IF
- PIT-UE-SPEECHRESEARCH-WH
- PIT-UE-STAYPOSITIVE-RESEARCH
- PIT-UE-SURGIRESEARCH-BW-X

Date/Time of Visit

NOW

☐ Historical Visit: a visit that occurred at some time in the past or at some other location (possibly non-VA) but is not used for workload credit.

Recent Lab Results

No Orders Found.

Vitals

Vital	Value	Date/Time
T	Refused	Jan 28, 2016 14:47
P	39	Jan 28, 2016 14:43
R	28	Jan 28, 2016 14:47
BP	88/50	Jan 28, 2016 14:47
HT	53 in	Jan 28, 2016 10:00 (134.62 cm)
WT	43 lb	Jan 28, 2016 10:00 (19.50 kg)
PN	8	Mar 17, 2016 10:46

Appointments/Visits/Admissions

No data found

Cover Sheet Problems Meds Orders Notes Consults Surgery D/C Summ Labs Reports

3:01 PM 8/19/2016

Step 7b

10. You will be returned to the Cover Sheet page. Date/Time of Visit will automatically populate showing you as the provider. (UESURBW/UEPTRES - Date - Provider: You)
11. At the bottom of the page, click the Notes tab

Vista CPRS in use by: Gilbert, Karen L. (vista.pittsburgh.med.va.gov)

File Edit View Tools Help

ZMZOUSE, MINNIE (OUTPATIENT) **UESURBW Aug 1** **Step 10**

000-00-9191 Jan 01, 1910 (106) Provider: GILBERT, KAREN L.

Flag Remote Data Postings WAD

Active Problems

- Dementia Nos (ICD-9-CM 294.8)
- Dementia With Lewy Bodies (ICD-9-CM 331.82)
- Copd (ICD-9-CM 496)
- Right Mass Chest (ICD-9-CM 793.9)
- Hypertension, Essential (ICD-9-CM 401.9)
- Carpal Tunnel Syndrome (ICD-9-CM 354.0)

Allergies / Adverse Reactions

- Cheddar Cheese
- Cal Dander
- Walnut
- Vancomycin
- Peanuts
- Nonsteroidal Anti-Inflammatory
- Cephalexin
- Sulfonamides
- Metoprolol (Lopressor)
- Morphine
- Doxycycline (Colace)
- Furosemide (Lasix)

Postings

- Allergies
- Research Study Alert - Warning
- Smoking Risk - Warning Aug 20, 2008
- Suicide Risk - Warning Dec 10, 2007
- Eligement Risk - Warning
- Advance Directive Nov 24, 2015

Active Medications

Medication	Status	Clinical Reminders	Due Date
Non-Va Zoprin 800mg Tab	Active	Adv Dir/Psych (BH Nurse/Provider)	DUE NOW
Non-Va Moxiprinol 500mg Tab	Active	Alcohol Screen (Nurse/Provider)	Sep 16, 15
Non-Va A & D Oint	Active	Tobacco Use Screen (Nurse/Provider)	Mar 30, 09
Non-Va Multivitamin Cap/Tab	Active	Depression Screen (Nurse/Provider)	DUE NOW
Non-Va Omeprazole 20mg Ec Cap	Active	Education/Communication (Nurse)	Jul 30, 14
Non-Va Belladonna Alk 0.13/Phenobarb 16mg/5ml	Active	Evaluation of + Depression Screen	DUE NOW
Non-Va Kava Cap/Tab	Active	Hep C Risk Screen (Nurse/Prov)	DUE NOW
Non-Va Belladonna Alk 0.13/Phenobarb 16mg/5ml	Active	Med Reconciliation (Provider)	Jul 09, 15
Non-Va St John's Wort Cap/Tab	Active	Pain Assessment (Nurse)	Jul 14, 15
Non-Va Atorvastatin 20mg Cap/Tab	Active	Pressure Ulcer Prevention (Nurse)	DUE NOW
Non-Va Garlic Oil Cap/Dial	Active	Pressure Ulcer Prevention (Prov)	DUE NOW
Non-Va No Reported Non-Va Med Use By Patient	Active	PTSD Screen (Nurse/Provider)	Nov 07, 14
Non-Va A & D Oint	Active	Evaluation of + PTSD Screen	DUE NOW
Non-Va Melatonin 3mg Cap/Tab	Active	Suicide Screen (BH Provider)	Dec 10, 08
Non-Va Melatonin 3mg Cap/Tab	Active	Abuse/Neglect Screen (Nurse/Prov)	DUE NOW
		Tetanus Toxoid Due (Nurse/Provider)	DUE NOW
		Homelessness Screening (Nurse/Prov)	DUE NOW
		My Healthiest Interest (Nurse/Prov)	DUE NOW
		Pneum13 (Nurse/Prov) Pneumococcal	DUE NOW
		Return to Clinic (Provider)	DUE NOW

Recent Lab Results

No Orders Found

Vitals

Vital	Value	Date/Time	Location
T	Refused	Jan 28, 2016 14:47	
P	39	Jan 28, 2016 14:43	LYING FEMORAL LEFT AT REST
R	28	Jan 28, 2016 14:47	
BP	88/50	Jan 28, 2016 14:47	
HT	53 in	Jan 28, 2016 10:00 (134.62 cm)	
WT	43 lb	Jan 28, 2016 10:00 (19.50 kg)	ACTUAL, STANDING WEIGHT
PN	8	Jan 28, 2016 10:00	

Appointments/Visits/Admissions

No data found

Navigation: Cover Sheet | Problems | Meds | Orders | Notes | **Notes**

Step 11

Windows Taskbar: 3:07 PM 8/19/2016

12. Choose New Note tab
13. Progress Note Properties Box will open
14. In the Progress Note Title, enter either RESEARCH STUDY ALERT – WARNING, RESEARCH INITIAL/CONSENT NOTE, RESEARCH NOTE, PHYSICAL THERAPY CONSULT - RESEARCH or PHYSICAL THERAPY - RESEARCH depending on the type of note you are entering.

The screenshot displays the Vista CPRS application window. The top menu bar includes File, Edit, View, Action, Options, Tools, and Help. The patient information bar shows ZZMOUSE, MINNIE (OUTPATIENT) with UESURBW Aug 19, 16 15:07 and Provider: GILBERT, KAREN L. The left sidebar lists various note types, with 'New Note' highlighted at the bottom. The main window shows a list of signed notes by date range. A 'Progress Note Properties' dialog box is open, showing the 'Progress Note Title' field with a dropdown menu. The dropdown menu is open, showing options like 'CHEMOTHERAPY ORAL/SUPPORTIVE MEDICATION ADMINISTRATION', 'EDUCATION RECORD', 'EDUCATION RECORD 1', 'EDUCATION/COMMUNICATION ASSESSMENT', 'EDUCATION/C...', 'NON-VA ADVANCE DIRECTIVE', 'NON-VA ADVANCE DIRECTIVE', 'NON-VA DISCHARGE SUMMARY', 'NON-VA DISCHARGE SUMM...', 'NON-VA POWER OF ATTORNEY', 'NON-VA POWER OF ATTORNEY', '0386 <VA CHOICE APPROVAL FOR MEDICAL CARE VA FORM...', and 'No Location'. The 'Date/Time of Note' is set to Aug 19, 2016@15:12, and the 'Author' is Gilbert, Karen L - CLINICAL RESEARCH COOF. A green arrow points to the 'New Note' tab with the label 'Step 12'. Another green arrow points to the 'Progress Note Properties' dialog box with the label 'Steps 13 and 14'.

15. Click OK or Enter

If fillable template appears – Close it – Click Yes twice on Cancel Dialog Processing Block – You will have a blank slate in which you can copy/paste/complete the appropriate note template. (Blank Word document templates are located on the Nerve Block Drive in the CPRS Note Templates Folder [Z:\Nerve_Block_Study\CPRS Note Templates]. Some clean-up of the templates will be necessary.)

Step 15

Pick one type of visit from template. Delete all others.

If no vitals were taken, delete "Blood Pressure/Pulse"

PT Staff: In Con Meds, enter "To be reviewed by Study Coordinator"

RESEARCH NOTE

NAME OF VISIT - CHOOSE ONE OF THE FOLLOWING:

- SCREENING VISIT
- BASLINE VISIT
- SCREENING/BASLINE VISIT
- DAY OF SURGERY - PRE
- SURGERY VISIT
- DAY OF SURGERY - POST
- SURGERY VISIT
- POST OF DAY 1, 2, 3, 4, 5
- MORNING QUESTIONNAIRE
- VISIT
- MORNING PT VISIT
- AFTERNOON PT VISIT
- WEEK 2 VISIT
- WEEK 6 VISIT

PATIENT'S NAME was seen today for the NAME OF VISIT for The Nerve Block Study. IF VITALS WERE TAKEN FOR THE VISIT, NOTE HERE. IF NOT, DELETE THIS SECTION.

Blood Pressure:

Pulse:

DESCRIBE WHAT HAPPENED AT THE VISIT. INCLUDE ALL INFORMATION RELEVANT TO THE POTENTIAL OUTCOME OF THE STUDY AND THAT VERIFIES INFORMATION COLLECTED DURING THE VISIT.

BEGINNING AT DAY OF SURGERY - PRE

Reviewed the following:

Concomitant Medications: Verified via chart review

Adverse Events:

Potential Study Endpoints:

Serious Adverse Events:

The patient was reminded to contact the Study Coordinator, Karen Gilbert, or Dr. Williams should s/he have any questions, concerns or needs additional information.

16. When done composing note, right click and select Sign Note Now

The screenshot displays the Vista CPRS application window. The title bar reads "Vista CPRS in use by: Gilbert,Karen L. (vista.pittsburgh.med.va.gov)". The menu bar includes File, Edit, View, Action, Options, Tools, and Help. The patient information bar at the top shows "ZZMOUSE,MINNIE (OUTPATIENT)" with ID "000-00-9191" and birth date "Jan 01,1910 (106)". The provider is "GILBERT,KAREN L." and the location is "UESURBW Aug 25,16 10:13".

The left sidebar contains a tree view of note types under "Last 250 Signed Notes (Total 279)". The main text area displays a "RESEARCH NOTE" for "Aug 25,2016@10:15" by "GILBERT,KAREN L.". The note content includes a header "POST OP DAY 2 - MORNING QUESTIONNAIRE VISIT" and a paragraph: "Minnie Mouse was seen today for the Post Op Day 2 Morning Questionnaire Visit for The Nerve Block Study." Below this, it lists questionnaires completed: SFMPQ2, SF8, QoR15, and ORSDS. Further down, it states: "During our visit, we reviewed the following: Concomitant Medications: Verified via chart review, Adverse Events: None reported by patient, Potential Study Endpoints: None reported by patient, Serious Adverse Events: None reported by patient." The note concludes with: "Patient is pleased with her care and is anxious to go home. Is confident that her hard work with the PT staff will pay off and is looking forward to returning to her busy lifestyle." and "The patient was reminded to contact the Study Coordinator, Karen Gilbert, or Dr. Williams should s/he have any questions, concerns or needs additional information."

A right-click context menu is open over the text "Sign Note Now...". The menu options include Cut (Ctrl+X), Copy (Ctrl+C), Paste (Ctrl+V), Reformat Paragraph (Shift+Ctrl+R), Find in Selected Note, Replace Text, Check Grammar, Check Spelling, Copy into New Template, Add to Signature List, Delete Progress Note..., Edit Progress Note..., Make Addendum..., Save without Signature, Sign Note Now..., Identify Additional Signers, Preview/Print Template (Ctrl+W), Insert Template (Ctrl+Ins), Edit Encounter Information (Ctrl+E), and View Consult Details (Shift+Ctrl+U). A green arrow points to the "Sign Note Now..." option, labeled "Step 16".

The bottom status bar shows "Cover Sheet | Problems | Meds | Orders | Notes | Consults | Surgery | D/C Summ | Labs | Reports". The taskbar at the bottom shows the Windows Start button and several application icons. The system clock in the bottom right corner shows "11:13 AM 8/25/2016".

- 17.Primary Encounter Provider Box will open
- 18.Enter Williams,Brian A
- 19.Click OK or Enter

VistA CPRS in use by: Gilbert, Karen L (vista.pittsburgh.med.va.gov)

File Edit View Action Options Tools Help

ZZMOUSE, MINNIE (OUTPATIENT) UESURBW Aug 25, 16 10:13 No PACT assigned at any VA location /

000-00-9191 Jan 01, 1910 (106) Provider: GILBERT, KAREN L

Flag VistAWeb Remote Data Postings WAD

Last 250 Signed Notes (Total: 279) RESEARCH NOTE - PIT-UE SURGRESEARCH-BW-X, Gilbert, Karen L (Aug 25, 16@10:15)

Date	Title	Subject	Author	Location
Aug 19, 16	VACCINE/SKIN TEST DOCUMENTATION		Shearn, Pamela L	NON COUNT-X
Aug 19, 16	VACCINE/SKIN TEST DOCUMENTATION		Shearn, Pamela L	NON COUNT-X
Aug 19, 16	Adverse React/Allergy		Shearn, Pamela L	"No Location"
Aug 19, 16	Adverse React/Allergy		Shearn, Pamela L	"No Location"
Aug 01, 16	RESEARCH NOTE		Gilbert, Karen L	PIT-UE-SURGRESEARCH-BW-X
Jul 28, 16	RESEARCH NOTE		Gilbert, Karen L	PIT-UE-SURGRESEARCH-BW-X
Jul 28, 16	RESEARCH STUDY ALERT - WARNING		Gilbert, Karen L	PIT-UE-PITRESEARCH-WK-X
Jul 28, 16	RESEARCH INITIAL/CONSENT NOTE		Gilbert, Karen L	PIT-UE-SURGRESEARCH-BW-X
Apr 22, 16	SKIN ASSESSMENT	skin	Winters, David J	NON COUNT-X
Apr 22, 16	NURSING NOTE	testing	Winters, David J	NON COUNT-X
Apr 18, 16	NURSING NOTE		Shearn, Pamela L	NON COUNT-X
Mar 18, 16	PAIN INPATIENT		Price, Amber Jewel	NON COUNT-X
Mar 18, 16	SKIN ASSESSMENT		Price, Amber Jewel	NON COUNT-X
Mar 17, 16	Addendum to PULMONARY NEBULIZER TRAINING CONSULT		Shimek, Kimberly M	NON COUNT-X
Mar 17, 16	PULMONARY NEBULIZER TRAINING CONSULT		Shimek, Kimberly M	NON COUNT-X
Mar 01, 16	ADMISSION ASSESSMENT - NURSING		Shearn, Pamela L	NON COUNT-X

LOCAL TITLE: RESEARCH NOTE
STANDARD TITLE: RESEARCH NOTE
DATE OF NOTE: AUG 25, 2016@10:15 ENTRY DATE: AUG 25, 2016
AUTHOR: GILBERT, KAREN L EXP COSIGNER:
URGENCY: STATUS: UNSIGNED

POST OP DAY 2 - MORNING QUESTIONNAIRE VISIT

Minnie Mouse was seen today for the Post Op Day 2 Morning Q for The Nerve Block Study.

Patient completed the following questionnaires independent:

SNHG2
SF3
QoR15
ORSDS

During our visit, we reviewed the following:

Concomitant Medications: Verified via chart review
Adverse Events: None reported by patient
Potential Study Endpoints: None reported by patient
Serious Adverse Events: None reported by patient

Patient is pleased with her care and is anxious to go home. Is confident that her hard work with the PT staff will pay off and is looking forward to returning to her busy lifestyle.

The patient was reminded to contact the Study Coordinator, Karen Gilbert, or Dr. Williams should s/he have any questions, concerns or needs additional information.

Primary Encounter Provider

Please Select the Primary Provider for this Encounter.

OK Cancel

Williams, Brian A - Director/Impact Clinic
Williams, Anita G - Nurse Practitioner
Williams, Autumn D - Prosthetic Representative
Williams, Ayanna Lee - Registered Nurse
Williams, Brian A - Director/Impact Clinic
Williams, Carita N - Nursing Assistant
Williams, Darlene P - Nursing Assistant
Williams, David E - Health Care Tech
Williams, Deshaun D - Nursing Assistant
Williams, John P - Physician
Williams, Joseph Gregory - Resident
Williams, Lauren - Licensed Practical Nurse
Williams, Lauren - Physical Therapist (float)

Steps 17, 18 and 19

/ Templates
Encounter
New Note

Cover Sheet Problems Meds Orders Notes Consults Surgery D/C Summ Labs Reports

11:17 AM 8/25/2016

20. Missing Encounter Information Box will open

21. Click Yes or Enter

The screenshot shows the Vista CPRS interface. The top bar indicates the user is Gilbert, Karen L. (vista.pittsburgh.med.va.gov). The patient is ZZMOUSE, MINNIE (OUTPATIENT), DOB 000-00-9191, Jan 01, 1910 (106). The provider is GILBERT, KAREN L. The research note is titled 'RESEARCH NOTE, PIT-UE-SURG-RESEARCH-BW-X, Gilbert, Karen L. (Aug 25, 2016@10:15)'. The note is currently being edited. The left sidebar shows a list of medical categories, with 'Research Note' selected. The main window displays the research note content, including a table of previous notes and the current note text. A dialog box titled 'Missing Encounter Information' is open, displaying a warning icon and the message: 'This note title is marked to prompt for the following missing encounter information: A diagnosis. A visit type or procedure. Would you like to enter encounter information now?'. The dialog box has 'Yes' and 'No' buttons. A green arrow points to the dialog box with the text 'Steps 20 and 21'.

Date	Title	Subject	Author	Location
Aug 19, 16	VACCINE/SKIN TEST DOCUMENTATION		Shearn, Pamela L	NON COUNT-X
Aug 19, 16	VACCINE/SKIN TEST DOCUMENTATION		Shearn, Pamela L	NON COUNT-X
Aug 19, 16	Adverse React/Allergy		Shearn, Pamela L	"No Location"
Aug 19, 16	Adverse React/Allergy		Shearn, Pamela L	"No Location"
Aug 01, 16	RESEARCH NOTE		Gilbert, Karen L	PIT-UE-SURG-RESEARCH-BW-X
Jul 28, 16	RESEARCH NOTE		Gilbert, Karen L	PIT-UE-SURG-RESEARCH-BW-X
Jul 28, 16	RESEARCH STUDY ALERT - WARNING		Gilbert, Karen L	PIT-UE-PTRESEARCH-VK-X
Jul 28, 16	RESEARCH INITIAL/CONSENT NOTE		Gilbert, Karen L	PIT-UE-SURG-RESEARCH-BW-X
Apr 22, 16	SKIN ASSESSMENT	skin	Winters, David J	NON COUNT-X
Apr 22, 16	NURSING NOTE	testing	Winters, David J	NON COUNT-X
Apr 18, 16	NURSING NOTE		Shearn, Pamela L	NON COUNT-X
Mar 18, 16	PAIN INPATIENT		Pice, Amber Jewel	NON COUNT-X
Mar 18, 16	SKIN ASSESSMENT		Pice, Amber Jewel	NON COUNT-X
Mar 17, 16	Addendum to PULMONARY NEBULIZER TRAINING CONSULT		Shimek, Kimberly M	NON COUNT-X
Mar 17, 16	PULMONARY NEBULIZER TRAINING CONSULT		Shimek, Kimberly M	NON COUNT-X
Mar 01, 16	ADMISSION ASSESSMENT - NURSING		Shearn, Pamela L	NON COUNT-X

LOCAL TITLE: RESEARCH NOTE
STANDARD TITLE: RESEARCH NOTE
DATE OF NOTE: AUG 25, 2016@10:15 ENTRY DATE: AUG 25, 2016@10:15
AUTHOR: GILBERT, KAREN L EXP COSIGNER: UNASSIGNED
URGENCY: STATUS: UNASSIGNED

POST OP DAY 2 - MORNING QUESTIONNAIRE VISIT

Minnie Mouse was seen today for the Post Op Day 2 Morning Questionnaire Visit for The Nerve Block Study.

Patient completed the following questionnaires independently:

- SPMPQ2
- SFB
- QoR15
- ORSDS

During our visit, we reviewed the following:

- Concomitant Medications: Verified via chart review
- Adverse Events: None reported by patient
- Potential Study Endpoints: None reported by patient
- Serious Adverse Events: None reported by patient

Patient is pleased with her care and is anxious to go home. Is confident that her hard work with the PT staff will pay off and is looking forward to returning to her busy lifestyle.

The patient was reminded to contact the Study Coordinator, Karen Gilbert, or Dr. Williams should s/he have any questions, concerns or needs additional information.

22. Encounter Form for PIT-UE-SURGResearch-BW-X or PIT-UE-PTRESEARCH-VK-X will open.

- If you are entering a note on **PIT-UE-SURGResearch-BW-X** on a(n)
 - New patient** (RESEARCH STUDY ALERT – WARNING, RESEARCH INITIAL/CONSENT NOTE, first RESEARCH NOTE only), select New Patient (Type of Visit) and click on Problem Focus (Section Name). Do NOT choose a Modifier.
 - Established patient** (any other RESEARCH NOTE, PHYSICAL THERAPY CONSULT – RESEARCH or PHYSICAL THERAPY – RESEARCH notes), select Established Patient (Type of Visit) and click on Brief [RN Only] (Section Name). Do NOT choose a Modifier.
- If you are entering a note on **PIT-UE-PTRESEARCH-VK-X**, you will not need to complete the Visit Type tab.
- If there are any boxes that are NOT grayed out in the Visit Related To section, select No.

The screenshot displays the CPRS software interface. The main window shows the 'Encounter Form for PIT-UE-SURGResearch-BW-X (Aug 25, 2016 @ 10:13)'. A green arrow points to the 'Type of Visit' dropdown menu, which is set to 'ESTABLISHED PATIENT'. The 'Section Name' dropdown is set to 'Brief [RN Only]'. The 'Visit Related To' section is visible with various checkboxes. The 'Visit Type' dropdown is set to 'ESTABLISHED PATIENT'. The 'Section Name' dropdown is set to 'Brief [RN Only]'. The 'Visit Related To' section is visible with various checkboxes. The 'Visit Type' dropdown is set to 'ESTABLISHED PATIENT'. The 'Section Name' dropdown is set to 'Brief [RN Only]'. The 'Visit Related To' section is visible with various checkboxes.

23. Select the Diagnosis Tab

24. Select Other Diagnosis

The screenshot displays the VISTA CPRS interface. The main window shows a list of notes for patient ZZMOUSE, MINNIE. A green arrow labeled 'Step 23' points to the 'Diagnosis' tab in the 'Encounter' window. The 'Diagnosis' tab is active, showing a list of problem list items. A second green arrow labeled 'Step 24' points to the 'Other Diagnosis...' button at the bottom of the 'Diagnosis' tab.

Encounter Window (PIT-UE-SURG/RESEARCH-BW-X)

Visit Type	Diagnosis	Procedures	Vitals	Immunizations	Skin Tests	Patient Ed	Health Factors	Exams
Problem List Items	ABDOMINAL PAIN							
	AFTERCARE POST SURGERY							
	BENIGN LESIONS OF SKIN							
	BITE							
	BREAST-FEMALE							
	BREAST-MALE							
	CARDIOVASCULAR							
	CIRRHOSIS							
	COUTIS							
	CROHN'S							
	DIVERTICULITIS							
	DIVERTICULOSIS							
	ENT							
	GANGLION							
	SURGICAL							

Other Diagnosis...

Diagnosis Section

Problem List Items	ICD-9-CM	294.8
☐ Dementia NOS (ICD-9-CM 294.8)	294.8	
☐ Dementia with Lewy Bodies (ICD-9-CM 331.82)	331.82	
☐ COPD (ICD-9-CM 496)	496	
☐ RIGHT MASS CHEST (ICD-9-CM 799.9)	799.9	
☐ Hypertension, Essential (ICD-9-CM 401.9)	401.9	
☐ Caput Tumor Syndrome (ICD-9-CM 354.0)	354.0	

Other Diagnosis...

Diagnosis Section

Add to PL	Primary	Selected Diagnoses

Comments

During our visit, we reviewed the following questions:

- SYMPTOMS
- SFB
- QoR15
- CRSOS

Concomitant Medications: None reported

Adverse Events: None reported

Potential Study Endpoints: None reported

Serious Adverse Events: None reported

Patient is pleased with her care and is anxious to go home. Is confident that her hard work with the PT staff will pay off and is looking forward to returning to her busy lifestyle.

The patient was reminded to contact the Study Coordinator, Karen Gilbert, or Dr. Williams should s/he have any questions, concerns or needs additional information.

25. Enter “Research” in the Search for Diagnosis Box
26. Click Search or Enter
27. Click on Encounter for Examination for Normal Comparison and Control in Clinical Research Program
28. Click OK or Enter

The screenshot displays the Vista CPRS interface. At the top, the patient information for ZZMOUSE, MINNIE (OUTPATIENT) is shown, including the date of birth (000-00-9191) and the provider (GILBERT, KAREN L.). The main window shows a list of notes, with the 'RESEARCH NOTE' selected. A 'Lookup Diagnosis' dialog box is open, showing the search results for the term 'research'. The results list includes 'Encounter for Examination for Normal Comparison and Control in Clinical Research Program'. A green arrow points to the search field with the text 'Steps 25, 26 and 27'.

29. Select Procedures Tab
30. Select Other Procedures

The screenshot displays the VISTA CPRS software interface. The main window shows the 'Encounter Form' for a patient named ZZMOUSE, MINNIE (OUTPATIENT). The 'Procedures' tab is selected, and the 'BIOPSY/DEBRIDEMENT' procedure is highlighted. A green arrow labeled 'Step 29' points to the 'Procedures' tab, and another green arrow labeled 'Step 30' points to the 'Other Procedure...' button.

The interface includes a top menu bar with options like File, Edit, View, Action, Options, Tools, and Help. Below the menu bar, there is a patient information section with fields for Patient ID (000-00-9191), Date (Aug 29, 2016), Time (07:51), and Provider (GILBERT, KAREN L.).

The main content area is divided into several sections. On the left, there is a 'Last Signed Notes' list. In the center, there is a 'RESEARCH NOTE' list. On the right, there is a 'Procedures' list. The 'Procedures' list is currently selected, and it shows a list of procedures with checkboxes for selection. The 'BIOPSY/DEBRIDEMENT' procedure is highlighted.

At the bottom of the 'Encounter Form' window, there is a 'Quantity' field, a 'Selected Procedures' list, and buttons for 'OK', 'Cancel', 'Select All', and 'Remove'.

31. Enter Trial in the Search for Procedure Box
32. Click Search or Enter
33. Click on Services Provided as part of a Phase III Clinical Trial (non-Medicare Temporary National Code)
34. Click OK or Enter

The screenshot shows the Vista CPRS interface. The patient record for ZZMOUSE, MINNIE (OUTPATIENT) is displayed. The central area shows a table of research notes with columns for Date, Title, Subject, Author, and Location. The 'Lookup Procedure' dialog box is open, showing a search for 'trial'. The search results list various procedures, with 'Services Provided as part of a Phase III Clinical Trial (non-Medicare Temporary National Code)' selected. The description for this procedure is displayed below the list. A green arrow points to the search bar and the selected result, with the text 'Steps 31, 32 and 33'.

Date	Title	Subject	Author	Location
Aug 19, 16	VACCINE/SKIN TEST DOCUMENTATION		Shearn, Pamela L.	NON COUNT-X
Aug 19, 16	VACCINE/SKIN TEST DOCUMENTATION		Shearn, Pamela L.	NON COUNT-X
Aug 19, 16	Adverse React/Allergy		Shearn, Pamela L.	"No Location"
Aug 19, 16	Adverse React/Allergy		Shearn, Pamela L.	"No Location"
Aug 01, 16	RESEARCH NOTE		Gilbert, Karen L.	PIT-UE-SURG/RESEARCH-BW-X
Jul 28, 16	RESEARCH NOTE		Gilbert, Karen L.	PIT-UE-SURG/RESEARCH-BW-X
Jul 28, 16	RESEARCH STUDY ALERT -			PIT-UE-PT/RESEARCH-HK-X
Jul 28, 16	RESEARCH INITIAL/CONSEN			PIT-UE-SURG/RESEARCH-BW-X

Lookup Procedure

Search for Procedure:

trial

Select from one of the following items:

Term

- Blinded procedure for lumbar stenosis, percutaneous image-guided lumbar decompression (pilot) or placebo-control, performed in an approved coverage with evidence development (ced) clinical trial
- Documentation of medical reason(s) for not ordering a first or second generation cephalosporin for antimicrobial prophylaxis (e.g., patients enrolled in clinical trials, patients with documented infection prior to surgery, procedure of int
- Documentation of reasons for patient initiating maintenance hemodialysis with a catheter as the mode of vascular access (eg, patient has a maturing av/fist, time-limited trial of hemodialysis, patients undergoing palliative dialysis, other
- Documentation of system reason(s) for ordering an advanced brain imaging study (i.e., needed as part of a clinical trial, other clinician ordered the study)
- Injection, Baclofen, 50 mcg for Intrathecal Trial
- Lodging costs (e.g., hotel charges) for clinical trial participant and one caregiver/companion
- Meals for Clinical Trial Participant and one Caregiver/Companion (non-Medicare Temporary National Code)
- Noncovered Procedure(s) using Either no Anesthesia or Local Anesthesia only, in a Medicare Qualifying Clinical Trial, per Day
- Noncovered Surgical Procedure(s) using Conscious Sedation, Regional, General or Spinal Anesthesia in a Medicare Qualifying Clinical Trial, per Day
- Oncology: Practice Guidelines: Management Differs from Guidelines as A Result of Patient Enrollment in an Institutional Review Board Approved Clinical Trial (for use in a Medicare-Approved Demonstration Project)
- Percutaneous/open Implant of Neurostimulator Electrode Array(s), Subq (Peripheral Subq Field Stimulation), includes Imaging Guidance, when Performed, Cervical, Thoracic or Lumbar, for Trial, includes Removal at Conclusion of Trial Period
- Services Provided as part of a Phase I Clinical Trial
- Services Provided as part of a Phase III Clinical Trial (non-Medicare Temporary National Code)**
- Services Provided as part of Phase II Clinical Trial (non-Medicare Temporary National Code)
- Transportation costs to and from trial location and local transportation costs (e.g., fares for taxicab or bus) for clinical trial participant and one caregiver/companion

Description: Services Provided as part of a Phase III Clinical Trial (non-Medicare Temporary National Code)

OK Cancel

15 matches found.

SERIOUS ADVERSE EVENTS: none

Patient is pleased with her care and is anxious to go home. Is confident that her hard work with the PT staff will pay off and is looking forward to returning to her busy lifestyle.

The patient was reminded to contact the Study Coordinator, Karen Gilbert, or Dr. Williams should s/he have any questions, concerns or needs additional information.

35. Once these three areas (Visit Type/Diagnosis/Procedures) are complete, click OK or Enter
36. Sign Note box will open
37. Enter your Signature Code
38. Click OK or Enter

The screenshot displays the Vista CPRS software interface. The main window shows a list of notes on the left and a detailed view of a research note on the right. A 'Sign Note' dialog box is open in the foreground, prompting for a signature code. A green arrow points to the dialog box with the text 'Steps 36, 37 and 38'.

Sign Note Dialog Box:

Signature Code:

Buttons: OK, Cancel

Main Window Content:

Local Title: RESEARCH NOTE
 Standard Title: RESEARCH NOTE
 Date of Note: AUG 26, 2016@10:15
 Entry Date: AUG 26, 2016@10:15
 Author: GILBERT, KAREN L
 Exp Co-Signer:
 Urgency:
 Status: UNST

POST OP DAY 2 - MORNING QUESTIONNAIRE VISIT

Minnie Mouse was seen today for the Post Op Day 2 Morning Visit for The Nerve Block Study.

Patient completed the following questionnaires independently:

- SDMQ2
- SFS
- QoR15
- ORSDS

During our visit, we reviewed the following:

- Concomitant Medications: Verified via chart review
- Adverse Events: None reported by patient
- Potential Study Endpoints: None reported by patient
- Serious Adverse Events: None reported by patient

Patient is pleased with her care and is anxious to go home. Is confident that her hard work with the PT staff will pay off and is looking forward to returning to her busy lifestyle.

The patient was reminded to contact the Study Coordinator, Karen Gilbert, or Dr. Williams should s/he have any questions, concerns or needs additional

ESTABLISHED PATIENT Brief (RN Only)

Diagnosis: Encounter for Examination for Normal Comparison and Control in Clinical Research Program (ICD-10-CM Z00.6) (Primary)

Procedures: Services Provided as part of A Phase III Clinical Trial (non-Medicare Temporary National Code)

Buttons: / Templates, Encounter, New Note

Bottom Bar: Cover Sheet | Problems | Meds | Orders | Notes | Consults | Surgery | D/C Summ | Labs | Reports

System Tray: 11:44 AM, 8/25/2016

39. Note will be electronically signed by you
40. All notes are to be cosigned by Dr. Williams. (PHYSICAL THERAPY CONSULT – RESEARCH and PHYSICAL THERAPY – RESEARCH have “Expected Cosigner” imbedded. Skip to Step 46)
41. Right click on your note.
42. Select Identify Additional Signers

VistaA CPRS in use by: Gilbert, Karen L (vista.pittsburghmed.va.gov)

File Edit View Action Options Tools Help

ZZMOUSE MINNIE (OUTPATIENT) UESURBW Aug 25, 16 10:13 No PACT assigned at any VA location /
000-00-9191 Jan 01, 1910 (106) Provider: GILBERT, KAREN L

Flag VistaWeb Postings
Remote Data WAD

Last 250 Signed Notes Visit: 08/25/16 RESEARCH NOTE, PIT-UE-SURG-RESEARCH-BW-X, KAREN L GILBERT (Aug 25, 16@10:15)

LOCAL TITLE: RESEARCH NOTE
STANDARD TITLE: RESEARCH NOTE
DATE OF NOTE: AUG 25, 2016@10:15 ENTRY DATE: AUG 25, 2016@10:16:30
AUTHOR: GILBERT, KAREN L EXP COSIGNER:
URGENCY: STATUS: COMPLETED

POST OP DAY 2 - MORNING QUESTIONNAIRE VISIT

Minnie Mouse was seen today for the Post Op Day 2 Morning Questionnaire Visit for The Nerve Block Study.

Patient completed the following questionnaires independently:

STMPQ2
SF8
QoD15
GRSDS

During our visit, we reviewed the following:

Concomitant Medications: Verified via chart review
Adverse Events: None reported by patient
Potential Study Endpoints: None reported by patient
Serious Adverse Events: None reported by patient

Patient is pleased with her care and is anxious to go home. Is confident that her hard work with the PT staff will pay off and is looking forward to returning to her busy lifestyle.

The patient was reminded to contact the Study Coordinator, Karen Gilbert, or Dr. Williams should s/he have any questions, concerns or needs additional information.

/s/ KAREN L GILBERT
CLINICAL RESEARCH COORDINATOR
Signed: 08/25/2016 11:46

ESTABLISHED PATIENT Brief (PIN Only)
Diagnoses:
Encounter for Examination for Normal Comparison and Control in Clinical Research Program (ICD-10-CM Z00.6) (Primary)

Procedures:
Services Provided as part of A Phase III Clinical Trial (non-Medicare Temporary National Code)

Templates
Encounter
New Note

Cover Sheet Problems Meds Orders Notes Consults Surgery D/C Summ Labs Reports

11:47 AM
8/25/2016

43. In the Select or Enter Additional Signers box, enter Williams, Brian A

44. Click Add or Enter

45. Click OK

The screenshot displays the VistA CPRS interface. At the top, the patient is identified as ZZMOUSE, MINNIE (OUTPATIENT) with ID 000-00-9191. The visit is dated 08/25/16 at 10:13. The provider is GILBERT, KAREN L. The note is titled 'RESEARCH NOTE' and was entered on 08/25/16 at 10:15. The note content describes a 'MORNING QUESTIONNAIRE VISIT' for Minnie Mouse, who is participating in 'The Nerve Block Study'. It mentions that the patient completed questionnaires independently and reviewed various topics during the visit, including concomitant medications, adverse events, and potential study endpoints. The patient is noted to be pleased with her care and anxious to continue her work. The note is signed by KAREN L GILBERT, CLINICAL RESEARCH COORDINATOR, on 08/25/2016 at 11:46. A dialog box titled 'Identify Additional Signers' is open, showing a list of potential signers. A green arrow points to the entry 'Williams, Brian A - DIRECTOR-IMP' in the list, with the text 'Step 43' next to it. The dialog box also includes fields for 'Author (not editable)' (Gilbert, Karen L) and 'Expected Cosigner (not editable)', and buttons for 'Add', 'Remove', and 'Remove All'. The background shows the main note entry screen with a list of medical history items on the left and a bottom navigation bar with options like 'Cover Sheet', 'Problems', 'Med', 'Orders', 'Notes', 'Consults', 'Surgery', 'D/C Summ', 'Labs', and 'Reports'.

46. At the top of the page, click File

Step 46

File

ZZZ, MINNIE (OUTPATIENT) 08/25/16 10:15 (NOT AC) assigned at any VA location /
000-00-9157 Jan 01, 1910 (106) Provider: GILBERT, KAREN L

Flag VistA Web Postings
Remote Data WAD

Last 250 Signed Notes Visit 08/25/16 RESEARCH NOTE, PIT-UE-SURG/RESEARCH-BW-X, KAREN L GILBERT (Aug 25, 16@10:15)

LOCAL TITLE: RESEARCH NOTE
STANDARD TITLE: RESEARCH NOTE
DATE OF NOTE: AUG 25, 2016@10:15 ENTRY DATE: AUG 25, 2016@10:16:30
AUTHOR: GILBERT, KAREN L EXP COSIGNER:
URGENCY: STATUS: COMPLETED

POST OP DAY 2 - MORNING QUESTIONNAIRE VISIT

Minnie Mouse was seen today for the Post Op Day 2 Morning Questionnaire Visit for The Nerve Block Study.

Patient completed the following questionnaires independently:

STHQ2
SF8
QoR15
ORSDS

During our visit, we reviewed the following:

Concomitant Medications: Verified via chart review
Adverse Events: None reported by patient
Potential Study Endpoints: None reported by patient
Serious Adverse Events: None reported by patient

Patient is pleased with her care and is anxious to go home. Is confident that her hard work with the PT staff will pay off and is looking forward to returning to her busy lifestyle.

The patient was reminded to contact the Study Coordinator, Karen Gilbert, or Dr. Williams should s/he have any questions, concerns or needs additional information.

/s/ KAREN L GILBERT
CLINICAL RESEARCH COORDINATOR
Signed: 08/25/2016 11:46

Receipt Acknowledged By:
* AWAITING SIGNATURE * WILLIAMS, BRIAN A

ESTABLISHED PATIENT Brief (PIN Only)
Diagnoses:
Encounter for Examination for Normal Comparison and Control in Clinical Research Program (ICD-10-CM Z00.6) (Primary)

Procedures:
Services Provided as part of A Phase III Clinical Trial (non-Medicare Temporary National Code)

Cover Sheet Problems Meds Orders Notes Consults Surgery D/C Summ Labs Reports

11:54 AM
8/25/2016

47. Select Refresh Patient Information

The screenshot displays the Vista CPRS application window. The title bar indicates the user is 'Gilbert, Karen L.' at 'vista.pittsburgh.med.va.gov'. The menu bar includes File, Edit, View, Action, Options, Tools, and Help. A green arrow points to the 'Refresh Patient Information' option in the 'View' menu, with the text 'Step 47' overlaid. The main window shows a patient record for 'SUBRW Aug 25, 2016 10:13'. The record details include:

- CLINICAL TITLE: RESEARCH NOTE
- STANDARD TITLE: RESEARCH NOTE
- DATE OF NOTE: AUG 25, 2016@10:15 ENTRY DATE: AUG 25, 2016@10:16:30
- AUTHOR: GILBERT, KAREN L EXP COSIGNER:
- URGENCY: STATUS: COMPLETED

 The note content describes a 'POST OP DAY 2 - MORNING QUESTIONNAIRE VISIT' for 'Minnie Mouse', where the patient completed questionnaires and reviewed various topics including concomitant medications, adverse events, and study endpoints. The note is signed by 'KAREN L GILBERT, CLINICAL RESEARCH COORDINATOR' on 08/25/2016 at 11:46. The bottom of the window shows a taskbar with various application icons and a system clock indicating 11:57 AM on 8/25/2016.

48. Note will appear in reverse chronological order with all other patient notes.

The screenshot displays the VistA CPRS interface for user Gilbert, Karen L. The patient is ZZWMOUSE, MINNIE (OUTPATIENT), with ID 000-00-9191 and birth date Jan 01, 1910. The provider is GILBERT, KAREN L. The notes are listed in reverse chronological order, starting from August 25, 2016.

Date	Title	Subject	Author	Location
Aug 25, 16	RESEARCH NOTE		Gilbert, Karen L	PIT-UE-SURGE
Aug 19, 16	VACCINE/SKIN TEST DOCUMENTATION		Shearn, Pamela L	NON COUNT-X
Aug 19, 16	VACCINE/SKIN TEST DOCUMENTATION		Shearn, Pamela L	NON COUNT-X
Aug 19, 16	Adverse React/Allergy		Shearn, Pamela L	"No Location"
Aug 19, 16	Adverse React/Allergy		Shearn, Pamela L	"No Location"
Aug 01, 16	RESEARCH NOTE		Gilbert, Karen L	PIT-UE-SURGESEARCH-BW-X
Jul 28, 16	RESEARCH NOTE		Gilbert, Karen L	PIT-UE-SURGESEARCH-BW-X
Jul 28, 16	RESEARCH STUDY ALERT - WARNING		Gilbert, Karen L	PIT-UE-PTRESEARCH-VK-X
Jul 28, 16	RESEARCH INITIAL/CONSENT NOTE		Gilbert, Karen L	PIT-UE-SURGESEARCH-BW-X
Apr 22, 16	SKIN ASSESSMENT	skin	Winters, David J	NON COUNT-X
Apr 22, 16	NURSING NOTE	testing	Winters, David J	NON COUNT-X
Apr 18, 16	NURSING NOTE		Shearn, Pamela L	NON COUNT-X
Mar 18, 16	PAIN INPATIENT		Price, Amber Jewel	NON COUNT-X
Mar 18, 16	SKIN ASSESSMENT		Price, Amber Jewel	NON COUNT-X
Mar 17, 16	Addendum to PULMONARY NEBULIZER TRAINING CONSULT		Shimek, Kimberly M	NON COUNT-X
Mar 17, 16	PULMONARY NEBULIZER TRAINING CONSULT		Shimek, Kimberly M	NON COUNT-X
Mar 01, 16	ADMISSION ASSESSMENT - NURSING		Shearn, Pamela L	NON COUNT-X
Mar 01, 16	SKIN ASSESSMENT		Shearn, Pamela L	NON COUNT-X
Mar 01, 16	Adverse React/Allergy		Shearn, Pamela L	"No Location"

The detailed note content for the selected 'RESEARCH NOTE' (Aug 25, 2016) is as follows:

LOCAL TITLE: RESEARCH NOTE
 STANDARD TITLE: RESEARCH NOTE
 DATE OF NOTE: AUG 25, 2016@10:15 ENTRY DATE: AUG 25, 2016@10:16:30
 AUTHOR: GILBERT, KAREN L EXP COSIGNER:
 URGENCY: STATUS: COMPLETED

POST OP DAY 2 - MORNING QUESTIONNAIRE VISIT

Minnie Mouse was seen today for the Post Op Day 2 Morning Questionnaire Visit for The Nerve Block Study.

Patient completed the following questionnaires independently:

- SEMPQ2
- SF8
- QoR15
- ORSDS

During our visit, we reviewed the following:

- Concomitant Medications: Verified via chart review
- Adverse Events: None reported by patient
- Potential Study Endpoints: None reported by patient
- Serious Adverse Events: None reported by patient

Patient is pleased with her care and is anxious to go home. Is confident that her hard work with the PT staff will pay off and is looking forward to returning

ESTABLISHED PATIENT Brief (RN Only)

Diagnoses:
 Encounter for Examination for Normal Comparison and Control in Clinical Research Program (ICD-10-CM Z00.6) (Primary)

Procedures:
 Services Provided as part of A Phase III Clinical Trial (non-Medicare Temporary National Code)

RESEARCH INITIAL/CONSENT NOTE

PATIENT NAME consented to participation in the study titled: 4-drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty Analgesia in Veterans – THE NERVE BLOCK STUDY on **DATE** at **TIME**.

The research study was explained and informed consent was obtained by **NAME OF PERSON OBTAINING CONSENT**

The full consent document was reviewed with the patient and the patient verbalized understanding. The patient was given every opportunity to ask questions. The PI/Coordinator were able to answer all questions to the patient's satisfaction. Risks and potential study medication side effects were reviewed. Approximately **NOTE TIME SPENT (MINUTES/HOUR[S])** was spent explaining the study and the consent. A copy of the signed consent was given to the patient at the end of the study visit. No study procedures were conducted prior to informed consent.

The patient **IS/IS NOT** participating in another research study. **IF PATIENT IS PARTICIPATING IN ANOTHER RESEARCH STUDY IT MUST BE NOTED HERE. PATIENTS MAY NOT PARTICIPATE IN 2 GREATER THAN MINIMAL RISK STUDIES UNLESS APPROVED BY THE IRB. RESEARCH ALERT ON THE CHART NOT REQUIRED.**

The purpose of this research is to evaluate two different nerve block injection drugs given one time prior to surgery to try to control pain following Total Hip or Knee Arthroplasty. Patient's participation in this study could be as long as 3-4 months depending on how long after patient signs consent that surgery is scheduled. The last study visit will be 6 weeks after surgery.

If you need additional information please contact:

Brian Williams, MD, MBA, Principal Investigator

Office: 412-360-1602

Cell/Text: 412-721-1430

Karen Gilbert, Study Coordinator

Office: (412) 360-6666

Cell: (412) 518-1322

After Hours Research Answering Service: 1 (866) 785-9015

RESEARCH STUDY ALERT - WARNING

PARTICIPANT'S NAME is participating in the study titled 4-drug Nerve Block versus Plain Local Anesthetic for Knee and Hip Arthroplasty Analgesia in Veterans – THE NERVE BLOCK STUDY

This is a prospective randomized clinical trial evaluating two different nerve block injection drugs to try to control pain following Total Hip or Knee Arthroplasty. The study will specifically look at patient reported and physical therapy progress. Subjects will be randomized to receive plain bupivacaine or bupivacaine plus CBD (clonidine-buprenorphine-dexamethasone) one time prior to surgery. Patient's participation in this study could be as long as 3-4 months depending on how long after patient signs consent that surgery is scheduled. Last study visit will be 6 weeks after surgery.

For additional information please see the research study note dated **DATE OF RESEARCH NOTE**.

RESEARCH NOTE

NAME OF VISIT - CHOOSE ONE OF THE FOLLOWING:

- SCREENING VISIT
- BASELINE VISIT
- SCREENING/BASELINE VISIT
- DAY OF SURGERY – PRE SURGERY VISIT
- DAY OF SURGERY – POST SURGERY VISIT
- POST OP DAY 1, 2, 3, 4, 5.....
- MORNING QUESTIONNAIRE VISIT
- PHYSICAL THERAPY CONSULT – RESEARCH
- PHYSICAL THERAPY - RESEARCH
- WEEK 2 VISIT
- WEEK 6 VISIT

PATIENT'S NAME was seen today for the **NAME OF VISIT** for The Nerve Block Study.

IF VITALS WERE TAKEN FOR THE VISIT, NOTE HERE. IF NOT, DELETE THIS SECTION.

Blood Pressure:

Pulse:

DESCRIBE WHAT HAPPENED AT THE VISIT. INCLUDE ALL INFORMATION RELEVANT TO THE POTENTIAL OUTCOME OF THE STUDY AND THAT VERIFIES INFORMATION COLLECTED DURING THE VISIT.

BEGINNING AT DAY OF SURGERY – PRE

During our visit, we reviewed the following:

Concomitant Medications: Verified via chart review

Adverse Events: “None noted by patient” or Describe

Potential Study Endpoints: “None noted by patient” or Describe

Serious Adverse Events: “None noted by patient” or Describe

The patient was reminded to contact the Study Coordinator, Karen Gilbert, or Dr. Williams should **s/he** have any questions, concerns or needs additional information.

VAPHS Human Subjects Research Listing of Reportable Events

The following table has been created to assist investigators/study teams. The table outlines the types of events related to human subjects research that must be reported, the method/process to be followed to report, and the timeframes for reporting. If you encounter a problem or event that is not described on this table, or you are having difficulty determining when/if an event requires reporting, it is advised that you consult with the IRB Office (VHAPTHIRB@va.gov) as soon as possible. Please note that with the exception of Research Information Security Incidents, the procedures listed here are unique to studies overseen by the VAPHS IRB. If your study is overseen by the VA Central IRB, please follow their procedures.

SECTION A: EVENTS AND PROBLEMS REQUIRING IMMEDIATE ACTION		
Type of Event:	Examples:	How to submit:
Local Unexpected and Related Research Deaths	Any death of a research subject participating in research overseen by the VAPHS IRB determined by the PI/member of the study team to be unexpected and related to the research.	Oral report must be made immediately to the IRB Office at 412-360-2394 or 412-360-2396. If no one answers, a voice mail message must be left that includes: - The PI's name - The name of the study and study ID number - Date of the death A written notification must also be submitted to the IRB within 5 business days of becoming aware of the death. For studies in ProSPECT→Submit Reportable Event: Serious and Unexpected Adverse Event For studies in Paper → Submit Serious Adverse Event Report Note: These events must also be added to the Serious Adverse Event Log (in Table 2) and submitted at the time of Continuing Review.

SECTION A: EVENTS AND PROBLEMS REQUIRING IMMEDIATE ACTION (Continued)

Research Information Protection Incident	• Any information security incident related to VA research including, inappropriate access, loss or theft of PHI; noncompliant storage, transmission, removal or destruction of PHI; or theft, loss, or noncompliant destruction of equipment containing PHI. Examples may include, but are not limited to: ○ Inappropriate access, loss or theft of documents containing PHI (e.g., informed consent forms, HIPAA Authorization forms, case report forms) ○ Unauthorized destruction (accidentally or intentionally) of research records ○ Loss, theft or unauthorized destruction of equipment (e.g., laptops, other mobile devices, external storage media) containing VA research-related PHI ○ Transmission of VA research-related PHI not encrypted according to VA standards. ○ Use or connection of unauthorized equipment (e.g., non-VA thumb drive, unauthorized personally owned equipment) to store, process, or transmit VA research-related PHI ○ Malicious attack on or unauthorized access to VA information system containing VA research related PHI Note: Issues related to HIPAA Authorizations and deficiencies (such as invalid HIPAA Authorizations, deficient waivers of authorization, and other uses and disclosures of PHI for research without legal authority) are to be reported in accordance with SECTION B. RESEARCH INFORMATION PROTECTION INCIDENTS ARE TO BE REPORTED WITHIN 1 HOUR OF DISCOVERY	1. <u>Monday- Friday (7:00 am- 4:30 pm)</u> Submit an email to the VHAPTHRIPP@va.gov following the instructions outlined in Appendix A of VAPHS Policy 014, Research Information Incident Reporting. NOTE: Emails sent to this address MUST be sent from the VA network and must be encrypted. If you are NOT able to access the network, please contact the Research Office at 412-360-2384 or 412-360-2396 for instructions. 2. <u>If it is after 4:30 pm M-F or the weekend, you must call</u> the VAPHS Operator (412-822-2222) and ask for the Administrator on Duty (AOD) and inform the AOD that you need to report a Research Information Security Incident. The email as described in #1 (above) must also be sent on the next business day. 3. DO NOT SUBMIT anything to the IRB either in paper or via ProSPECT unless specifically instructed to do so by the IRB Staff.
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SECTION B: EVENTS AND PROBLEMS REQUIRING REPORTING WITHIN 5 BUSINESS DAYS

Type of Event:	Examples:	How to submit:
Serious Unexpected and Related Adverse Events	Any serious, unexpected local (internal) adverse event related to the research	For studies in ProSPECT→Submit Reportable Event: Serious and Unexpected Adverse Event Note: These events must also be added to the Serious Adverse Event Log (in Table 2) and submitted at the time of Continuing Review.
Serious Unanticipated and Related Problems	- Any situation that requires action on the part of the study team and/or sponsor to prevent an immediate hazard to subjects or others including: - Any change made to the study protocol without prior IRB approval when the change was made in order to eliminate an apparent immediate hazard to subjects or others. - Any problem described in a VA Pharmacy Benefits Management (PBM) alert relevant to local human subjects. - Any Data Monitoring Committee (DMC), Data Safety Monitoring Board (DSMB), or Data Safety Monitoring Committee (DSMC) report describing a safety problem. - Any sponsor analysis describing a safety problem. NOTE: Sponsor AE reports lacking meaningful analysis do not fall under this category. - Any work related injury to personnel involved in human research, or any research-related injury to any other person, that requires more than minor medical intervention (i.e., basic first aid), requires extended surveillance of the affected individual(s), or leads to serious complications or death. - Any other incident or problem or combination of problems that present a genuine risk of substantive harm to the safety rights, or welfare of human research subjects, research personnel, or others, or that substantively compromise the VAPHS Human Research Protection Program (HRPP). Specific examples, include but are not limited to: - Failure to obtain/complete any safety labs or monitoring as dictated by the protocol.	For studies in ProSPECT→Submit Reportable Event: Serious Unanticipated Problem

SECTION B: EVENTS AND PROBLEMS REQUIRING REPORTING WITHIN 5 BUSINESS DAYS (continued)

Type of Event:	Examples:	How to submit:
Serious Unanticipated and Related Problems (continued from previous page)	- o Change in FDA labeling due to new risks, or withdrawal from marketing of a drug, device or biologic used in a research protocol. - o Inclusion of participants who do not meet eligibility criteria - o Failure to report incidental findings of clinical significance to a participant's responsible clinician and/or the participant. - o External Adverse Event report which the investigator/study team feels raises a safety concern. - o Finding by an external/sponsor monitor of a safety problem¹	For studies in ProSPECT→Submit Reportable Event: Serious Unanticipated Problem
Apparent Serious/Apparent Continuing Non-Compliance	• Initiation of VA human subjects research without IRB approval • Initiation of VA human subjects research without R&D committee approval. • Initiation of VA human subjects research without written notification from the ACOS/R&D that the project may begin. • Substantive Informed Consent and/or HIPAA deficiencies including: - o Use of an informed consent document whose content was not approved by the VAPHS IRB. This includes: ▪ Crossing out approved language ▪ Adding language that has not yet been approved ▪ Use of the wrong version of the consent (i.e., not the one currently approved by the IRB) - o Printer errors that result in content from the approved version not appearing on the printed version (i.e., text is missing - o 10 or more participants signing a consent form lacking the IRB approval stamp/watermark. - o Initiation of research interactions or interventions with one or more subjects prior to obtaining IRB-approved written informed consent or IRB-approved verbal consent or a waiver of informed consent. - o Conducting a specific research procedure or procedures for which the subject did not give consent (e.g., consent form requires that subjects check a box if willing to participate and subject does not check the box and procedures are done anyway). - o Failure to obtain informed consent for one or more subjects (where required, unless waived by the IRB).	For studies in ProSPECT→Submit Reportable Event: Non-Compliance NOTE: If the event or problem being reported is a previously unreported Serious Unexpected Adverse Event or Serious Unanticipated Problem (e.g., it was not reported within 5 business days) please follow the Serious Unexpected Adverse Event or Serious Unanticipated Problem reporting submission instructions.

¹ If no written report is available at the time that the study team is initially notified of the safety problem, a follow-up report, with a copy of the written report, must be submitted to the IRB (as a Reportable Event-Other) upon receipt.

SECTION B: EVENTS AND PROBLEMS REQUIRING REPORTING WITHIN 5 BUSINESS DAYS (continued)

Type of Event:	Examples:	How to submit:
Apparent Serious/Apparent Continuing Non-Compliance (continued from previous page)	- o Failure to obtain documentation of informed consent (where required, unless waived by the IRB). This includes: ▪ Consent document was never signed by participant or witness, if required (i.e., blank signature line) - o Failure to obtain HIPAA Authorization for one or more subjects (where required, unless waived by the IRB). This includes: ▪ Original HIPAA Authorization not retained/lost by study team - o HIPAA Authorization was never signed by the participant (i.e., blank signature line) - o Accessing medical records to determine if a potential participant is eligible when that participant has not signed a HIPAA Authorization or a Waiver of HIPAA Authorization has not been granted by the IRB. Note this includes when the HIPAA Authorization signature line is missing and/or blank. - o Sharing individually identifiable information with anyone not authorized to receive it per the study protocol, consent and/or HIPAA Authorization. - o Providing individually identifiable private information to a collaborator, study sponsor, or other entity when: a) such disclosure was not described in the signed HIPAA Authorization, b) valid HIPAA authorization was not obtained, or c) a waiver of HIPAA Authorization allowing such disclosure was not granted by the IRB. Note this includes when the HIPAA Authorization signature line is missing and/or blank. - o Providing more individually identifiable private information to a collaborator, study sponsor, or other entity than was described in the HIPAA authorization signed by the participant or was described in the approved HIPAA waiver. • Continuation of human research beyond the specified IRB approval period (i.e., the IRB approval expiration date) except where in the subjects' best interests as determined by the IRB Chair. • Making changes to the study protocol without IRB approval when the change is NOT being made to eliminate an apparent immediate hazard to subjects or others. • Failure to implement, in a timely fashion, any protocol or informed consent modifications or other changes required by the IRB.	For studies in ProSPECT→Submit Reportable Event: Non-Compliance NOTE: If the event or problem being reported is a previously unreported Serious Unexpected Adverse Event or Serious Unanticipated Problem (e.g., it was not reported within 5 business days) please follow the Serious Unexpected Adverse Event or Serious Unanticipated Problem reporting submission instructions.

SECTION B: EVENTS AND PROBLEMS REQUIRING REPORTING WITHIN 5 BUSINESS DAYS (continued)

	• Failure to notify the IRB of a death, SAE, or problem as required. • Failure to remediate any noncompliance in a timely fashion as required by the IRB. • Conduct of research without required credentialing, privileging, or initial training. • Conduct of international research. • Conduct of research involving children or women known to be pregnant, without the required approvals. (Either CRADO- pre March 2015 or MCD- post March 2015). • Involvement of prisoners in VA research without CRADO approval² • Any finding of apparent serious noncompliance as listed here, by any entity, including clinical trial monitors. • Unfounded labeling of a death, SAE, or problem as “anticipated” or “not related” to the research. • Any combination of noncompliant actions that collectively present a genuine risk of substantive harm to the safety, rights, or welfare of human research subjects, research personnel or others, or substantively compromises the VAPHS HRPP. • Substantive deviations from IRB approved protocols, including substantive violations of inclusion or exclusion criteria	
Local (VAPHS) investigator initiated suspension or termination of VAPHS IRB Approved Research	• VAPHS PI decides to temporarily stop enrollment or some/all study procedures on his/her study due to safety concerns (for subjects, personnel, or others) • VAPHS PI decides to permanently stop all study procedures due to safety concerns (for subjects, personnel, or others)	For studies in ProSPECT→Submit Reportable Event: Suspension or Termination
Study sponsor or external (outside of VAPHS) entity initiated Suspensions or Terminations of VAPHS IRB Approved Research	• VAPHS PI receives notification from study sponsor or external entity to temporarily stop enrollment or some/all study procedures due to safety concerns (for subjects, personnel, or others) • VAPHS PI receives notification from study sponsor or external entity to permanently stop all study procedures due to safety concerns (for subjects, personnel, or others)	For studies in ProSPECT→Submit Reportable Event: Suspension or Termination

² Investigators/Study Teams should contact the IRB Office mailgroup (VHAPTHIRB@va.gov) to discuss any instance in which a subject has been incarcerated PRIOR to making a report of non-compliance. Contact with the IRB should be initiated within 1 business day of when the study team becomes aware to ensure that should follow up reporting be necessary, there is adequate time. Please refer to VAPHS Guidance on Incarceration of VAPHS Research Participants for specific instruction.

SECTION C: EVENTS AND PROBLEMS REQUIRING REPORTING AT THE TIME OF CONTINUING REVIEW

Type of Event:	Specific Examples	How to submit:
Internal Serious Adverse Events	• <u>Greater than minimal risk studies</u> must report Internal Serious Adverse Events ▪ deemed to be unexpected and not related ▪ deemed to be expected and related ▪ deemed to be expected and not related • <u>Minimal risk studies</u> must report Internal Serious Adverse Events ▪ deemed to be expected and related	These events should be logged on the Serious Adverse Event Log (in Table 3) and submitted with the continuing review.
Protocol Deviations/Violations which do not pose an increased risk of harm to study participants, research staff or others.	• Missed study visits or visits occurring outside of the timeframe dictated in the protocol when the missed visits do not include any safety labs, tests, or safety monitoring. • Missed specimen collection or collection occurring outside of the timeframe dictated in the protocol when the specimens are not being collected for safety purposes. • Failure to administer a survey/questionnaire dictated by the protocol provided that the survey is not being administered to ensure/assess subject physical or psychological safety. • Lack of protocol adherence by study participant when the lack of adherence does not increase the risk of harm to the study participant. • Printer errors on the consent form in which all approved text is present but the formatting is different than the approved version (e.g., one page prints on two pages instead). • Printer/copier errors which result in the IRB approval stamp/watermark missing for less than 10 participants (NOTE: If 10 this occurs for 10 or more participants, this must be reported as apparent serious/continuing non-compliance within 5 business days) • Lack of a CPRS warning flag (when required by the IRB) (NOTE: If occurs for 10 or more participants, this must be reported as apparent serious/continuing non-compliance within 5 business days)	These events should be logged on the Protocol Deviation Log and submitted with the continuing review.
OTHER	• External Monitoring Reports which DO NOT describe a safety problem • Sponsor Correspondence which DOES NOT describe a safety problem, if the sponsor requires that it be reported to the IRB. • Data Safety Monitoring Board (DSMB) reports NOT describing a safety problem	These events can be uploaded at the time of continuing review.

SECTION D: EVENTS AND PROBLEMS WHICH DO NOT REQUIRE REPORTING

Type of Event:	Specific Examples
External Adverse Events ³	• External safety reports received from study sponsors which lack any meaningful analysis. • Any reports of adverse events occurring at sites other than VAPHS when VAPHS is the coordinating site. • Any reports of adverse events occurring at sites other than VAPHS when VAPHS is a participating site.

³ If a VAPHS investigator has a significant concern regarding an external adverse event, a report can be submitted as a Serious Unanticipated Problem. Should a study sponsor require that external AEs be acknowledged by the IRB, these events can be submitted to the IRB at the time of continuing review. The information contained on the reports will need to be documented via the VAPHS External Adverse Event Log, or a comparable form that contains all of the information on the AE Log, and uploaded in ProSPECT. Studies in paper can attach the External AE Log to the continuing review submission.

LIST OF ACRONYMS USED IN PROTOCOL

ACOS	Assistant Chief of Staff
AE	Adverse Event
CARS	Compliance Activity Review Subcommittee
CBD	Clonidine-Buprenorphine-Dexamethasone
CEX	Clinical Exam Form
CFR	Code of Federal Regulations
Co-I	Co-Investigator
CPRS	Computerized Patient Record System
CRF	Case Report Form
CRNA	Certified Registered Nurse Anesthetists
CTC	Clinical Trials Center
DoD	Department of Defense
DOS	Day of Surgery
ECO-HSR	Education and Compliance Office for Human Subject Research (University of Pittsburgh)
FDA	Food and Drug Administration
FIM	Functional Independence Measure
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
IDS	Investigational Drug Service
IMPACT Clinic	Interdisciplinary Medical Preoperative Assessment Consultation and Treatment Clinic
IND	Investigational New Drug
IRB	Institutional Review Board
ISO	Information Safety Office(r)
MMPNA	MultiModal PeriNeural Analgesia
MOP	Manual of Operating Procedures
MSA	Medical Support Assistant
PFNS	Preservative Free Normal Saline
PI	Principal Investigator
PID	Patient Identification Number
Pitt PT	University of Pittsburgh Physical Therapist
PO	Privacy Officer
R & D	Research and Development
SAE	Serious Adverse Event
SC	Study Coordinator
SID	Study Identification Number
SIV	Site Initiation Visit
SOC	Standard of Care
TARF	Treatment Allocation Request Form
VA PT	Veterans Administration Physical Therapist
VAPHS	Veterans Administration - Pittsburgh Healthcare System
VAPHS RCO	Veterans Administration – Pittsburgh Healthcare System Research Compliance Office(r)
VHA	Veterans Health Administration

NERVE BLOCK MOP CHANGE LOG**Version 1.0 – October 20, 2016**

VERSION	DATE	MOP CHANGES
1.0	August 1, 2016	Original
1.1	August 15, 2016	1. Addition of Research Publication language 2. Addition of Replacement Block Assignment language
1.2	September 26, 2016	1. Clarification of Falls language 2. General format clean-up
1.3	October 20, 2016	1. Updated Appendix 14: CPRS – Chart Note Templates and Entry Instructions 2. Addition of Appendix 17: Nerve Block MOP Change Log