



## HRP-592 - Protocol for Human Subject Research with Use of Test Article(s)

**Protocol Title:** Pain with trigger finger injection: A comparison of steroid alone versus steroid/lidocaine mixture

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### 1.0 Objectives

#### 1.1 Study Objectives

- Compare pain, using a visual analog scale (VAS), associated with corticosteroid/lidocaine injection (CSL) to corticosteroid injection alone (CS) and corticosteroid/saline (CSS) injection.
- Review any adverse events related to the three treatment groups (CSL, CS and CSS).
- Review the efficacy of the three treatment groups (CSL, CS and CSS).
- Subcategorize patients based on demographic variables, comorbid conditions and anatomic location.

#### 1.2 Primary Study Endpoints

- Compare pain and efficacy associated with the three treatment groups.
  - VAS and mean daily pain values

#### 1.3 Secondary Study Endpoints

- Incidence of adverse effects
- Presence of clicking/locking (yes/no)
- Patient satisfaction (yes/no)
- Time to stopping medication
- Need for additional analgesics
- Effectiveness of injection

### 2.0 Background

#### 2.1 Scientific Background and Gaps

Trigger finger, or stenosing tenosynovitis, is a condition in which the flexor tendon is prohibited from gliding through the tendon sheath because of thickening of the synovial sheath over the tendon.<sup>1</sup> As a result, digital movement is impaired, and the affected digit locks in either flexion (the most common position) or extension, resulting in pain and swelling. Trigger digit pathology can be associated with

occupations involving lifting or gripping, but it also is associated with systemic disease states, such as rheumatoid arthritis and diabetes mellitus.<sup>2</sup> Trigger finger has a reported incidence of 28 cases per 100,000 subjects annually, or a risk of 2.6% over a lifetime.<sup>3</sup> A survey of 516 patients treated between 1975 and 1994 indicated that 61% of trigger fingers occurred in women.<sup>4</sup>

Multiple approaches are available for both operative and non-operative management of trigger finger. Splinting, corticosteroids (either single or multiple injections), percutaneous surgery, and open surgery are all established means of treatment. A single injection of corticosteroid can provide symptom relief in 47% to 87% of patients with trigger finger.<sup>7-11</sup> According to Newport et al,<sup>13</sup> each additional corticosteroid injection resulted in diminished efficacy. Corticosteroid injection has been widely accepted as first line treatment.<sup>8,9,14-16</sup> When splinting and/or corticosteroid injections fail, surgery is recommended.<sup>14</sup> Lidocaine is commonly used in conjunction with a corticosteroid because of its local anesthetic effect and near-immediate relief of pain. This dilution and increase in overall volume can aid in confirmation of medication delivery to the appropriate tissue and encourage diffusion of the steroid crystalline suspension to the entire area of interest. Though corticosteroids have a relatively quick onset of action, it may take 24 - 48 to notice symptom relief related to their prolonged anti-inflammatory effect, therefore lidocaine usually provides immediate, although, short-acting relief of pain. Lidocaine is extremely painful upon injection and may be an unnecessary addition to the steroid suspension. Addition of lidocaine also increases the volume of the injection, which may be a source of pain upon deposition into the flexor tendon sheath and subcutaneous tissues of the finger.

## 2.2 Previous Data

Previous studies have evaluated the efficacy of steroid injections as compared to placebo injections in the treatment of trigger finger but no previous studies have compared steroid/lidocaine injections to injections without lidocaine. The aim of this study is to compare post-injection pain and efficacy of trigger finger injection using a combination of lidocaine/corticosteroid versus corticosteroid injection alone or corticosteroid/saline (equal volume). Our hypothesis is that lidocaine causes unnecessary pain upon injection and does not improve the efficacy of the steroid in providing sustained anti-inflammatory benefit. We also seek to determine if volume of injection plays a role in immediate post-injection pain (corticosteroid/saline group).

## 2.3 Study Rationale

See study objectives

# 3.0 Inclusion and Exclusion Criteria

## 3.1 Inclusion Criteria

- Age: 18 – 90
- Gender: male or female (non-pregnant)
- Clinically diagnosed trigger digit
- Subject is able to provide voluntary, written informed consent
- Subject, in the opinion of the clinical investigator, is able to understand the clinical investigation and is willing to perform all study procedures and follow-up visits.

## 3.2 Exclusion Criteria

- Age: <18 or >90
- Pregnant or lactating women
- Non-English speaking individuals
- Medication contradictions to lidocaine, corticosteroids and/or saline
- History of multiple drug allergies
- Prior injection or surgery on the affected finger
- Diagnosis of reflex sympathetic dystrophy (RSD) or complex regional pain syndrome (CRPS)
- Open wound

- Inability to provide informed consent

### **3.3 Early Withdrawal of Subjects**

#### **3.3.1 Criteria for removal from study**

Patients will be withdrawn from the study for safety reasons including severe adverse reactions, failure of subject to adhere to protocol requirements, or subject consent withdrawal.

#### **3.3.2 Follow-up for withdrawn subjects**

If a patient is withdrawn from the study, data collection will be terminated from that time point forward. All prior data collected will be included in the analysis. These subjects will not be replaced, but instead more subjects may need to be enrolled. These new data will be recorded and analyzed as would any other new enrollee. No further follow-up of withdrawn subjects is necessary.

## **4.0 Recruitment Methods**

### **4.1 Identification/Recruitment of subjects**

Subjects will be identified as part of their initial or routine evaluation by one of the study investigators in the Bone & Joint Institute.

### **4.2 Recruitment materials – N/A**

### **4.3 Eligibility/screening of subjects**

Adult patients presenting to the Bone & Joint Institute will be evaluated as part of standard of care. Those subjects meeting eligibility requirements will be presented with the opportunity to participate in the research study by a member of the research team.

## **5.0 Consent Process and Documentation**

### **5.1 Consent Process**

#### **5.1.1 Obtaining Informed Consent**

##### **5.1.1.1 Timing and Location of Consent**

Subjects presenting to the study investigator's practice site as part of their initial or routine evaluation will be given the opportunity to participate in the research study. Patients will be given information about the study and asked to participate. If eligible, based on inclusion and exclusion criteria, informed consent will be obtained at the time of the screening visit and the patient will be enrolled in the study.

##### **5.1.1.2 Coercion or Undue Influence during Consent**

Subjects will be given ample time to read and review the consent form on their own. All questions the patient may have will be answered and written consent will be obtained. A member of the research team will assist in the explanation and obtaining of the written consent. A copy of the signed consent will be given to the patient and another copy sent to Medical Records.

#### **5.1.2 Waiver or alteration of the informed consent requirement – N/A**

### **5.2 Consent Documentation**

**5.2.1 Written Documentation of Consent**

A member of the research team will assist in the explanation and obtaining of the written consent. A copy of the signed consent will be given to the patient and another copy sent to Medical Records.

**5.2.2 Waiver of Documentation of Consent – N/A****5.3 Consent – Other Considerations****5.3.1 Non-English Speaking Subjects – N/A****5.3.2 Cognitively Impaired Adults - N/A****5.3.2.1 Capability of Providing Consent - N/A****5.3.2.2 Adults Unable To Consent - - N/A****5.3.2.3 Assent - N/A****5.3.3 Subjects who are not yet adults (infants, children, teenagers)****5.3.3.1 Parental Permission - N/A****5.3.3.2 Assent – N/A****6.0 HIPAA Research Authorization and/or Waiver or Alteration of Authorization****6.1 Authorization and/or Waiver or Alteration of Authorization for the Uses and Disclosures of PHI****Check all that apply:**

- Authorization will be obtained and documented as part of the consent process.
- Partial waiver is requested for recruitment purposes only (*Check this box if patients' medical records will be accessed to determine eligibility before consent/authorization has been obtained*)
- Full waiver is requested for entire research study (*e.g., medical record review studies*)
- Alteration is requested to waive requirement for written documentation of authorization

**6.2 Waiver or Alteration of Authorization for the Uses and Disclosures of PHI****6.2.1 Access, use or disclosure of PHI representing no more than a minimal risk to the privacy of the individual****6.2.1.1 Plan to protect PHI from improper use or disclosure**

Information is included in Section 10 of this protocol

**6.2.1.2 Plan to destroy identifiers or a justification for retaining identifiers**

The list will be destroyed upon completion of the study.

**6.2.2 Explanation for why the research could not be practicably be conducted without access to and use of PHI**

Patient identifiers are necessary for identification and review of the patient's medical records. A unique study code number will be used for identification of study data. The linking list will be destroyed upon completion of the study.

**6.2.3 Explanation for why the research could not practicably be conducted without the waiver or alteration of authorization – N/A****6.3 Waiver or alteration of authorization statements of agreement**

Protected health information obtained as part of this research 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 permitted uses and disclosures according to federal regulations.

The research team will collect only information essential to the study and in accord with the 'Minimum Necessary' standard (information reasonably necessary to accomplish the objectives of the research) per federal regulations.

Access to the information will be limited, to the greatest extent possible, within the research team.

All disclosures or releases of identifiable information granted under this waiver will be accounted for and documented.

**7.0 Study Design and Procedures****7.1 Study Design**

This will be a prospective, randomized, double-blind study in which patient and data collector is blinded to the treatment protocol. The physician who is preparing and performing the injection will remain unblinded.

Recruitment → Randomization → Treatment (Corticosteroid v corticosteroid/lidocaine v corticosteroid/saline)

Corticosteroid (CS) → post-injection assessment immediately following injection → post-injection assessment at 6 weeks (via phone)

Corticosteroid/lidocaine (CSL) combination → post-injection assessment immediately following injection → post-injection assessment at 6 weeks (via phone)

Corticosteroid/saline (CSS) combination → post-injection assessment immediately following injection → post-injection assessment at 6 weeks (via phone)

**7.2 Study Procedures****7.2.1 Visit 1 – Screening/Baseline Visit**

Patients will be given information about the study and asked to participate. If eligible, based on inclusion and exclusion criteria, informed consent will be obtained at the time of the screening visit and the patient will be enrolled in the study.

After obtaining informed consent, the patient will be randomized to one of three treatment groups. The study investigator (who is unblinded) will randomly draw a sealed envelope

containing one of the three treatment groups. The sealed envelopes will be stored in a secure area within the clinic practice site.

- CS – corticosteroid alone -1 cc dexamethasone (4mg/ml) only
- CSL – corticosteroid/lidocaine combination - 1 cc dexamethasone (4mg/ml) and 1 cc 1% lidocaine
- CSS – corticosteroid/saline combination - 1 cc dexamethasone (4mg/ml) and 1 cc 0.9% injectable saline)

The patient will then be asked to complete a Patient Survey pre-injection (VAS Pain Scale and Trigger question). The study investigator will perform a single injection using a 25 gauge 1.5” needle. The needle will be inserted at 90 degrees to the skin, 1 cm proximal to the metacarpophalangeal joint flexion crease. The injections will be prepared in the Bone & Joint Institute as part of standard of care.

The patient will then complete the Patient Survey at 1 minute and 10 minutes following injection (VAS Pain Scale and Trigger question).

Objective hand exam will be performed including range of motion at MP, PIP and DIP joints, presence of clicking or locking, triggering score, pain with range of motion and grip strength as part of the patient’s standard of care.

### 7.2.2 6-Week Follow-Up Phone Call

The patient will be contacted via phone and will be asked to verbally complete the Patient Survey (patient will be asked to report the VAS Pain score over the phone in .5 increments – i.e. 3.5, 4.0, 5.0, 5.5, etc.) and the coordinator will record the score. The patient will also answer question about how often he/she triggers (see phone script).

### 7.2.3 Study Visit Flowsheet

Screening Visit – Visit 1	6-Week Follow-Up – Phone Call
Enrollment, Randomization, Pre-injection VAS, Injection, Post-injection VAS x 2, objective hand exam (SOC)	VAS, trigger question

### 7.3 Duration of Participation

Subjects will only be seen in the clinic site once (time of enrollment in study) and will be contacted via telephone six weeks post-injection.

### 7.4 Test Article(s) (Study Drug(s) and/or Study Device(s))

#### 7.4.1 Description

The study drugs consist of the following:

- CS – corticosteroid alone -1 cc dexamethasone (4mg/ml) only
- CSL – corticosteroid/lidocaine combination - 1 cc dexamethasone (4mg/ml) and 1 cc 1% lidocaine
- CSS – corticosteroid/saline combination - 1 cc dexamethasone (4mg/ml) and 1 cc 0.9% injectable saline)
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All of these drugs are currently FDA approved and considered standard of care.

#### **7.4.2 Treatment Regimen**

The study investigator will perform a single injection using a 25 gauge 1.5” needle. The needle will be inserted at 90 degrees to the skin, 1 cm proximal to the metacarpophalangeal joint flexion crease.

#### **7.4.3 Method for Assigning Subject to Treatment Groups**

Patients will be randomized to receive CS, CSL, or CSS during their clinic visit.

#### **7.4.4 Subject Compliance Monitoring**

After obtaining informed consent, patients will be randomized to one of three recruitment groups. They will then be asked to complete a Patient Survey pre-injection and again 1 minute and 10 minutes after injection. They will be contacted via phone at six weeks post-injection and asked to verbally complete the Patient Survey.

#### **7.4.5 Blinding of the Test Article**

The three drug combinations will be compounded in the Bone & Joint Institute as part of routine standard of care.

#### **7.4.6 Receiving, Storage, Dispensing and Return**

##### **7.4.6.1 Receipt and Storage of Test Article**

The compounds will be stored at room temperature in the Bone & Joint Institute. These injections are routine standard of care and all policies regarding receipt, storage, dispensing and disposing will be strictly followed.

##### **7.4.6.2 Preparation and Dispensing**

Subject randomization will be performed prior to dispensing of any study drugs. After randomization, subjects will be dispensed study drugs as follows:

- CS – corticosteroid alone -1 cc dexamethasone (4mg/ml) only
- CSL – corticosteroid/lidocaine combination - 1 cc dexamethasone (4mg/ml) and 1 cc 1% lidocaine
- CSS – corticosteroid/saline combination - 1 cc dexamethasone (4mg/ml) and 1 cc 0.9% injectable saline)

##### **7.4.6.3 Return or Destruction of the Test Article**

The study drug will be disposed of in clinic following standard procedure for disposal of needles.

##### **7.4.6.4 Prior and Concomitant Therapy**

See exclusion criteria

## **8.0 Data and Specimen Banking For Future Undetermined Research**

**8.1 Data and/or specimens being stored – N/A**

**8.2 Location of storage – N/A**

**8.3 Duration of storage – N/A**

**8.4 Access to data and/or specimens – N/A**

**8.5 Procedures to release data or specimens – N/A**

## 8.6 Process for returning results– N/A

# 9.0 Statistical Plan

## 9.1 Sample size determination

Sample size was determined based on a review of prior studies that used the VAS as the main outcome tool. A total sample size of 221 was determined based on the number needed to detect a difference of 5 mm assuming a standard deviation of 10 mm in the VAS and when also considering a 15 % drop out rate. 221 total patients initially enrolled in the study would account for 64 patients per treatment arm (Corticosteroid only v corticosteroid/lidocaine v corticosteroid/saline). Public Health Sciences will be ensuring accuracy of statistical analyses. Stratification based on perioperative variables of interest will not be necessary in our study. Instead, we will be analyzing these variables via subgroup multivariate analyses at the conclusion of the study.

## 9.2 Statistical methods

The daily average pain score (VAS) will be compared between groups using either t-test or Wilcoxon test for each of the 6 days after the operation. Chi-square tests will be used to compare treatment groups for categorical variables (satisfaction, presence of clicking/locking, adverse events). Level of significance will be set at  $p < 0.05$ .

Secondary statistical analysis will include multivariate analyses to determine which variables such as anatomic location and comorbidities will impact the VAS score or modify the efficacy of injection. These can be accomplished by adding these variables and their interaction with treatment groups in the regression model. As these are secondary analysis, any interesting findings will be subject to validation in future studies.

Any deviations from the previously described statistical plan will be described and justified in a protocol amendment.

All analyses comparing the treatment groups will be conducted on an intention-to-treat basis. Two-tailed tests will be used at all times.

There will be an interim analysis when 50 % of patients (n=111) are enrolled and have completed final visit testing.

# 10.0 Confidentiality, Privacy and Data Management

## 10.1 Confidentiality

### 10.1.1 Identifiers associated with data and/or specimens

See the Research Data Plan Review Form

#### 10.1.1.1 Use of Codes, Master List

See the Research Data Plan Review Form

### 10.1.2 Storage of Data and/or Specimens

See the Research Data Plan Review Form

### 10.1.3 Access to Data and/or Specimens

See the Research Data Plan Review Form

### 10.1.4 Transferring Data and/or Specimens

See the Research Data Plan Review Form



## 10.2 Privacy

See the Research Data Plan Review Form

# 11.0 Data and Safety Monitoring Plan

## 11.1 Periodic evaluation of data

The research coordinator will complete the appropriate report form and logs; assist the principal investigator to prepare reports and notify the IRB and any applicable reporting agencies of all unanticipated problems / adverse events.

The research coordinator and principal investigator will confirm that all adverse events are correctly entered in the AE log; be available to answer any questions concerning AEs; notify the IRB and any applicable reporting agencies of unanticipated problems and AEs as appropriate. All assessments of AEs will be made by a licensed medical professional who is an investigator on the research.

## 11.2 Data that are reviewed

Data to be reviewed includes the VAS scale as well as incidence of adverse effects, and patient satisfaction.

## 11.3 Method of collection of safety information

Data will be collected beginning after informed consent at time of enrollment through six weeks postoperatively. Data will be collected at the initial clinic visit and again via telephone six weeks post-injection. Adverse events will be collected as they occur.

## 11.4 Frequency of data collection

Data will be collected beginning after informed consent at time of enrollment through six weeks postoperatively.

## 11.5 Individual's reviewing the data

All data will be reviewed by members of the research team at completion of study. Reporting of any adverse events will be reviewed as they occur.

## 11.6 Frequency of review of cumulative data

There will be an interim analysis in this study after 50% of patients are enrolled and have completed all study requirements. Adverse events will be reviewed as they occur.

## 11.7 Statistical tests

See statistical plan.

## 11.8 Suspension of research

There will be no stopping rules in this study as all medications are FDA approved and safe for patient use.

If a patient, at any point in the course of their treatment demonstrates a significant adverse event related to the study medication, then the adverse event will be addressed.

# 12.0 Risks

- Loss of confidentiality will be minimized as the research team will only have access to the research data and all information will be kept on a password-protected computer or in a locked filing cabinet.
- Subjects will be assigned to a treatment program by chance. The treatment received may prove to be less effective or to have more side effects than the other research treatment(s) or other available treatments.

- Allergic reaction to lidocaine or the preservative used in lidocaine.
- Nerve damage for a period of time after the injection.

## 13.0 Potential Benefits to Subjects and Others

### 13.1 Potential Benefits to Subjects

The treatment received may prove to be less or more effective or to have more side effects than the other research treatment or other available treatments.

### 13.2 Potential Benefits to Others

The results of this study will guide future treatment decisions.

## 14.0 Sharing Results with Subjects – N/A

## 15.0 Economic Burden to Subjects

### 15.1 Costs

All procedures are standard of care.

### 15.2 Compensation for research-related injury

It is the policy of the institution to provide neither financial compensation nor free medical treatment for research-related injury. In the event of injury resulting from this research, medical treatment is available but will be provided at the usual charge. Costs for the treatment of research-related injuries will be charged to subjects or their insurance carriers.

## 16.0 Number of Subjects

Approximately 222 people (74 per treatment arm) will be enrolled in this research study at the Hershey Medical Center.

## 17.0 Resources Available

### 17.1 Facilities and locations

Penn State Milton S. Hershey Medical Center

### 17.2 Feasibility of recruiting the required number of subjects – N/A

### 17.3 PI Time devoted to conducting the research

Sufficient time will be devoted to conducting the research and reviewing the data

### 17.4 Availability of medical or psychological resources – N/A

### 17.5 Process for informing Study Team

All team members have been given copies of all IRB approved documents – protocol, data collection tools, approval memos, etc. The team meets regularly to review data and any updates.

## 18.0 Other Approvals

This study was approved by the PSHMC Scientific Review Committee on 3/4/2015 prior to IRB submission.

## 19.0 Subject Stipend (Compensation) and/or Travel Reimbursements

N/A

## 20.0 Multi-Site Research – N/A

20.1 Communication Plans – N/A

20.2 Data Submission and Security Plan – N/A

20.3 Subject Enrollment – N/A

20.4 Reporting of Adverse Events and New Information – N/A

20.5 Audit and Monitoring Plans – N/A

## 21.0 Adverse Event Reporting

### 21.1 Adverse Event Definitions

<b>Adverse event</b>	Any untoward medical occurrence associated with the use of the drug in humans, whether or not considered drug related
<b>Adverse reaction</b>	Any adverse event caused by a drug
<b>Suspected adverse reaction</b>	Any adverse event for which there is a reasonable possibility that the drug caused the adverse event. Suspected adverse reaction implies a lesser degree of certainty about causality than “adverse reaction”. <ul style="list-style-type: none"> <li><i>Reasonable possibility.</i> For the purpose of IND safety reporting, “reasonable possibility” means there is evidence to suggest a causal relationship between the drug and the adverse event.</li> </ul>
<b>Serious adverse event or Serious suspected adverse reaction</b>	Serious adverse event or Serious suspected adverse reaction: An adverse event or suspected adverse reaction that in the view of either the investigator or sponsor, it results in any of the following outcomes: Death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.
<b>Life-threatening adverse event or life-threatening suspected adverse reaction</b>	An adverse event or suspected adverse reaction is considered “life-threatening” if, in the view of either the Investigator (i.e., the study site principal investigator) or Sponsor, its occurrence places the patient or research subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that had it occurred in a more severe form, might have caused death.
<b>Unexpected adverse event or Unexpected suspected adverse reaction.</b>	An adverse event or suspected adverse reaction is considered “unexpected” if it is not listed in the investigator brochure, general investigational plan, clinical protocol, or elsewhere in the current IND application; or is not listed at the specificity or severity that has been previously observed and/or specified.

**For device studies, incorporate the following definitions into the below responses, as written:**

<b>Unanticipated</b>	Any serious adverse effect on health or safety or any life-threatening problem or
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<b>adverse device effect</b>	death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or IDE application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.
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## 21.2 Recording of Adverse Events

All adverse events (serious or non-serious) and abnormal test findings observed or reported to study team believed to be associated with the study drug will be followed until the event (or its sequelae) or the abnormal test finding resolves or stabilizes at a level acceptable to the investigator.

An abnormal test finding will be classified as an adverse event if one or more of the following criteria are met:

- The test finding is accompanied by clinical symptoms
- The test finding necessitates additional diagnostic evaluation(s) or medical/surgical intervention; including significant additional concomitant drug treatment or other therapy  
**Note:** Simply repeating a test finding, in the absence of any of the other listed criteria, does not constitute an adverse event.
- The test finding leads to a change in study drug dosing or discontinuation of subject participation in the clinical research study
- The test finding is considered an adverse event by the investigator.

## 21.3 Causality and Severity Assessments

The investigator will promptly review documented adverse events and abnormal test findings to determine 1) if the abnormal test finding should be classified as an adverse event; 2) if there is a reasonable possibility that the adverse event was caused by the study drug(s) or device(s); and 3) if the adverse event meets the criteria for a serious adverse event.

If the investigator's final determination of causality is "unknown and of questionable relationship to the study drug(s) or device(s)", the adverse event will be classified as associated with the use of the study drug(s) or device(s) for reporting purposes. If the investigator's final determination of causality is "unknown but not related to the study drug(s) or device(s)", this determination and the rationale for the determination will be documented in the respective subject's case history.

## 21.4 Reporting of Adverse Reactions and Unanticipated Problems to the FDA

### 21.4.1 Written IND Safety Reports – N/A

### 21.4.2 Telephoned IND Safety Reports – Fatal or Life-threatening Suspected Adverse Reactions – N/A

## 21.5 Reporting Adverse Reactions and Unanticipated Problems to the Responsible IRB

In accordance with applicable policies of The Pennsylvania State University Institutional Review Board (IRB), the investigator will report, to the IRB, any observed or reported harm (adverse event) experienced by a subject or other individual, which in the opinion of the investigator is determined to be (1) unexpected; and (2) probably related to the research procedures. Harms (adverse events) will be submitted to the IRB in accordance with the IRB policies and procedures.

## 21.6 Unblinding Procedures – N/A

## 21.7 Stopping Rules

There are no stopping rules in this study as all medications are FDA approved and safe for patient use.

## 22.0 Study Monitoring, Auditing and Inspecting

### 22.1 Study Monitoring Plan

#### 22.1.1 Quality Assurance and Quality Control

Study data will be recorded and kept in the Research Coordinator's office, on a password protected computer. The Principal Investigator will oversee all aspects of the study.

#### 22.1.2 Safety Monitoring

The **Principal Investigator** will confirm that all adverse events (AE) are correctly entered into the AE case report forms by the coordinator; be available to answer any questions that the coordinators may have concerning AEs; and will notify the IRB, FDA, sponsor and/or DSMB of all applicable AEs as appropriate. All assessments of AEs will be made by a licensed medical professional who is an investigator on the research.

The **research coordinator** will complete the appropriate report form and logs; assist the PI to prepare reports and notify the IRB, FDA, and/or DSMB of all Unanticipated Problems/SAE's.

## 23.0 References

Saldana MJ: Trigger digits: Diagnosis and treatment. *J Am Acad Orthop Surg* 2001;9:246-252.

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Marks MR, Gunther SF: Efficacy of cortisone injection in treatment of trigger fingers and thumbs. *J Hand Surg [Am]* 1989;14:722-727.

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Murphy D, Failla JM, Koniuch MP: Steroid versus placebo injection for trigger finger. *J Hand Surg [Am]* 1995;20:628-631.

Maneerit J, Sriworakun C, Budhraj N, Nagavajara P: Trigger thumb: Results of a prospective randomized study of percutaneous release with steroid injection versus steroid injection alone. *J Hand Surg [Br]* 2003;28: 586-589.

## 24.0 Appendix – N/A