Toward Thriving Study

HUM00176302

Study Protocol

V1.6

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MPIs

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Contents

1. Protocol Summary

1.1. Synopsis

Title:	Toward Thriving Study
Grant Number:	N/A
Study Description:	A longitudinal clinical trial in a cohort of chronic pain to assess feasibility of a new behavioral intervention based on the principles of positive psychology. The study will recruit 20 participants, who will complete 4 timepoints (T1-T4). Participants will be consented at T1. T2 will be a kickoff meeting for all participants. After T2, participants will complete study intervention phase 1 (cultural probe kit) for three weeks. Next participants will participate in a facilitated workshop at T3, complete phase 2 of the intervention, followed by an exit interview at T4. Participants will complete a study survey at T1 and T4.
Objectives*:	The purpose of this pilot study is to introduce and test a positive psychology intervention meant to empower chronic pain patients and help support their resiliency and thriving.
Endpoints*:	1. Primary: Feasibility and acceptability of the behavioral intervention (cultural probe kit related activities). Percent (%) of participants engaging in the intervention between T1 and T4 2. Secondary: Change in PGIC between T1 and T4 Change in PROMIS Pain Interference between T1 and T4 3. Exploratory: Change in PROMIS 29 depression, anxiety sleep, fatigue between T1 and T4
Study Population:	Participants over the age of 18 with chronic pain
Description of Sites/Facilities Enrolling Participants:	This study will recruit patients at the Michigan Medicine. There will be no sites outside of the US.
Description of Study Intervention/Experimental Manipulation:	Participants will complete a cultural probe kit over 3-weeks. This kit is a design research tool, to prompt participants to document, map, journal, and reflect on various aspects of their daily lives
Study Duration*:	12 months
Participant Duration:	4 months

1.2. Schema

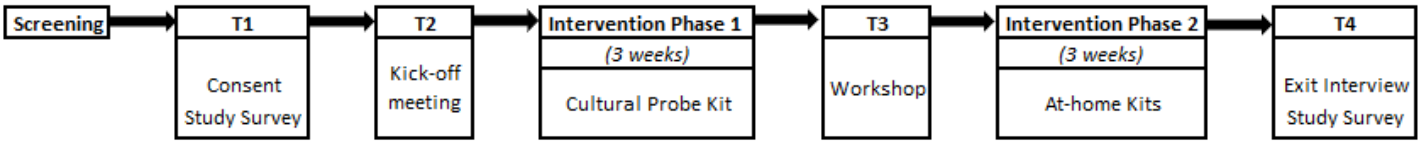

Figure 1 Study Schema

1.3. Schedule of Activities (SOA)

Table 1 Study SOA

	Screening	T1	T2	T3	T4
Screening	x				
Consent		x			
Demographics		x			
PROMIS 29-+ 2		x			x
PGIC					x

Chronic Pain Conditions		X			
Facilitated Interview			x		x

2. Introduction

2.1. Objective

The purpose of this pilot study is to introduce and test a positive psychology intervention meant to empower chronic pain patients and help support their resiliency and thriving.

2.2. Specific Aims

Testing the efficacy of a custom-designed set of reflective tools (plus interactive workshop) to empower chronic pain patients and help them envision a personal path to thriving.

2.3. Background

'Large studies in Europe, North America, Australasia, and other regions disclose that one in five of the adult population suffers from chronic moderate to severe pain [1] ,' yet there are societal misconceptions about what it means to live with chronic pain. Chronic pain sufferers encounter frequent barriers and few supports to help them live meaningful lives. This project has the potential to provide support to patients through positive psychology methods.

2.4. Methodology

Participants will be using a cultural probe kit, a design research tool, to prompt participants to document, map, journal, and reflect on various aspects of their daily lives. During an interactive, in-person workshop, participants will review and synthesize the contents of their probe kit and set goals for themselves. The workshop, which takes place after participants have completed three weeks of at-home activities, will be facilitated in small groups by a designer and psychologist team. Participants will end the study with 3-weeks of at-home activities and an exit interview about their experience. Specific instructions, as delivered in each week of the probe kit materials, as well as plans for the kickoff meeting, workshop and exit interview, follow.

3. Study Population

3.1. Inclusion Criteria

- Persistent or recurrent pain lasting longer than 3 months
- Age 18+
- Able to read and write English

3.2. Exclusion Criteria

- Cancer
    - History of any bone-related cancer or cancer that metastasized to the bone
    - Currently in treatment for any cancer or plan to start cancer treatment in the next 12 months
    - History of any cancer treatment in the last 24 months
- Active substance abuse
- Uncontrolled depression or psychosis
- Visual or hearing difficulties that would preclude participation
- Individuals started receiving disability or compensation within the past year, or currently involved in litigation
- Current/planned (in the next 2 years) enrollment in another study of a device or investigational drug that would interfere with this study, this may include participation in a blinded trial.
- Any other diseases or conditions that would make a patient unsuitable for study participation as determined by the site principal investigators. This would include but not be limited to severe psychiatric disorders, active suicidal ideations or history of suicide attempts, and an uncontrolled drug and/or alcohol addiction)

3.3. Screen Failures

Screen failures are defined as participants who consent to participate in the clinical trial but are later to found to be ineligible. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants, to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any serious adverse event (SAE).

3.4. Strategies for Recruitment and Retention

3.4.1. Methods of Recruitment

Participants will be screened and recruited through Michigan Medicine via the following methods:

1. In-person recruitment through Back and Pain Center (B&PC)
2. Umhealthresearch.com
3. Data direct queries
4. Flyers in clinic across Michigan Medicine
5. B&PC new patient registry APOLO HUM00041820

3.4.2. Recruitment and Enrollment

Participants will be tracked and screened using REDCap, a HIPAA compliant electronic data capture system. Those patients who meet eligibility criteria will be consented electronically through REDCap. They will then be asked to complete a study survey via REDCap and scheduled for future visits.

3.4.3. Incentives

Participants will be paid up to $250. They will receive $150 for completing the workshop (T3) and associated intervention phase 1 kit and $100 for completing the exit interview and associated phase 2 activities

4. Study Intervention

4.1. Overall

Participants will complete two phases of the study intervention before and after the T3 visit. The interventions are made up of self-guided at home activities.

4.2. Phase 1 and Workshop (T3)

Participants will be using a cultural probe kit, a design research tool, to prompt participants to document, map, journal, and reflect on various aspects of their daily lives. During an interactive, in-person workshop (T3), participants will review and synthesize the contents of their probe kit and set goals for themselves. The workshop, which takes place after participants have completed three weeks of at-home activities, will be facilitated in small groups by a designer and psychologist team.

4.3. Phase 2 and Exit Interview (T4)

Participants will end the study with 3-weeks of at-home activities and an exit interview about their experience. T4 may be completed in-person or virtually and maybe recorded.

5. Statistical Design and Analysis

5.1. Acceptability Study

We will conduct semi-structured interviews to understand participant perception of the intervention at T4. We will assess the proportion of participants who report that the intervention was relatively easy to understand after orientation, low burden (easy to do), and potentially effective.

5.1.1. Hypothesis

$\geq$80% of participants will report that the intervention was relatively easy to understand after orientation, low burden, and potentially effective.

5.1.2. Outcome

The primary outcome is the patient assessment of the cultural probe tool and the overall experience including orientation and facilitated workshop. A series of prompts in the semi-structured interview will elicit opinions about the intervention, the ease of completion, and the possibility that it could help promote positive emotions and resilience.

5.1.3. Hypothesis test and power analysis

Hypotheses tests are two-sided performed at the 5% significance level. 95% confidence interval will be conducted.

5.2. Feasibility Study

We will collect data related to the number of participants approached and consented; the percentage consented who attend the facilitated workshop, the number of activities the participants at the workshop have completed, the number of participants who take part in the exit interview and the progress made towards goals set at the Sensemaking Workshop. We will also explore the intervention's potential to improve patient-reported outcomes including patient global impression of change (PGIC). Patient-reported outcomes will be measured before and after the intervention.

5.2.1. Hypothesis

≥80% of participants attending the facilitated workshop will have completed at least 2 of the 3 reflective tools.

5.2.2. Outcome

The primary outcome is the proportion of participants who attending the Sensemaking Workshop have completed at least 2 of the 3 reflective tools. The secondary outcomes are patient's belief about the efficacy of intervention (PGIC) and other symptoms including pain interference, depression, anxiety, and sleep, etc. The rate of patients being lost-to-follow-up will also be tracked to aid in appropriate design of a future randomized clinical trial.

5.2.3. Hypothesis test and power analysis

Frequencies will be calculated related to feasibility data (e.g., number of participants approached, consented, and take part in the workshop). Descriptive statistics of patient-reported outcomes will be calculated before and after the intervention. Paired t-tests are used on patients' changes from T1 to T4. Wilcoxon test will be applied if departure from the assumption of normality. Hypotheses tests are two-sided performed at the 5% significance level. 95% confidence interval will be conducted. Power analysis for efficacy is based on t-tests.

6. Study Intervention Discontinuation and Participant Discontinuation/Withdrawal

6.1. Discontinuation of Study Intervention

Discontinuation from the intervention will be considered withdrawal from the study as well. This is further described below.

6.2. Participant Discontinuation/Withdrawal from the Study

Participants are free to withdraw from participation in the study at any time upon request.
An investigator may discontinue or withdraw a participant from the study for the following reasons:

- Significant study intervention non-compliance
- If any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant
- Disease progression which requires discontinuation of the study intervention
- If the participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

The reason for participant discontinuation or withdrawal from the study will be recorded on the off-study Case Report Form (CRF). Subjects who sign the informed consent form but do not receive the study intervention may be replaced. Subjects who sign the informed consent form, and receive the study intervention, and subsequently withdraw, or are withdrawn or discontinued from the study, will not be replaced.

6.3. Lost to Follow-Up

A participant will be considered lost to follow-up if he or she fails to complete the study visits and scheduled surveys and are unable to be contacted by the study site staff after three attempts at any point in the study.

The following actions must be taken if a participant fails to return to the clinic for a required study visit:

- The site will attempt to contact the participant and reschedule the missed visit within a 2-week timeframe and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study.

- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 3 telephone calls, text message and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's study record.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

7. Study Assessments and Procedures

7.1. Efficacy Assessments

All study evaluations are listed in section **Error! Reference source not found.**. Screening will occur the day of the T1 study visit. The T1 study visit will include consenting and completion of the study survey.

7.2. Safety and Other Assessments

As this is a minimal risk study, there are very few safety risks anticipated. Study staff will review the study risks with the participant during consent and answer any questions. Participants can withdraw at any time if they feel discomfort.

7.3. Adverse Events, Serious Adverse Events and Unanticipated Problems

7.3.1. Definition of Adverse Events (AE)

Adverse event means any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related (21 CFR 312.32 (a)).

7.3.2. Definition of Serious Adverse Events (SAE)

An adverse event (AE) or suspected adverse reaction is considered "serious" if, 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,
- 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 participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

7.3.3. Classification of an Adverse Event

7.3.3.1. Severity of Event

For adverse events (AEs) not included in the protocol defined grading system, the following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".]

7.3.3.2. Relationship to Study Intervention

All adverse events (AEs) must have their relationship to study intervention assessed by the PI who examines and evaluates the participant based on temporal relationship and clinical judgment. The degree of certainty about causality will be graded using the categories below.

- **Related** – The AE is known to occur with the study intervention, there is a reasonable possibility that the study intervention caused the AE, or there is a temporal relationship between the study intervention and event.

Reasonable possibility means that there is evidence to suggest a causal relationship between the study intervention and the AE.

- **Not Related** – There is not a reasonable possibility that the administration of the study intervention caused the event, there is no temporal relationship between the study intervention and event onset, or an alternate etiology has been established.

7.3.3.3. Expectedness

Study staff will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study intervention.

7.3.3.4. Time Period and Frequency for Event Assessment and Follow-Up

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during study visits and interviews of a study participant or upon review by a study monitor.

All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate case report form (CRF). Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

Study staff will record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

7.3.4. Adverse Event Reporting

Reporting timeline for this study is described in Table 2. Unrelated AEs will not be reported.

7.3.5. Serious Adverse Event Reporting

A timeline for reporting AEs, SAEs, UaPs and Protocol deviations to the Institutional Review Board of the University of Michigan are described in Table 2.

Table 2 Timeline for Reporting Study Events to IRB

Event	UM IRB
Non-serious Adverse Events	Will not be reported
Serious Adverse Events (Unrelated)	Will not be reported
Serious Adverse Event *(Related)*	Within 7 days of occurrence notification
Serious Adverse Event (Anticipated)	Annual report to IRB prior to scheduled continuing review
Non-serious adverse events grade 2 or higher *(moderate or greater)*	Annual report to IRB prior to scheduled continuing review
Privacy violation or breach of confidentiality	Report to IRB within 7 days Within 24 hours to the UMHS Privacy Office
Protocol deviations	Annual report to IRB prior to scheduled continuing review

7.4. Unanticipated Problems (UaP)

The Office for Human Research Protections (OHRP) considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

7.4.1. Unanticipated Problem Reporting (UaP)

The investigator will report unanticipated problems (UaPs) to the reviewing Institutional Review Board (IRB) and lead principal investigator (PI). The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UaP;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UaP.

To satisfy the requirement for prompt reporting, UPs will be reported using the timeline described in **Error! Reference source not found.**.

7.5. Risk/Benefit Assessment

7.5.1. Known Potential Risks

The known potential risks in this study are no more than mild risk level. The table below describes the specific risks for this study.

Table 3 Potential Study Risks

Risks	
Questionnaires	Survey questions about pain, emotions, and thinking patterns about pain will be administered as part of this study. Some participants may feel minor discomfort sharing information about their physical and mental health.
Breach of Confidentiality	Even with extensive protections in place, there is a very unlikely possibility of breaches in confidentiality. This will be considered a severe adverse event and will be reported to the IRB within 7 days.

7.5.2. Known Potential Benefits

Participants might benefit from being in the study by taking time and having structures to examine their supports and barriers, enhance positive emotions, gain health education, and clarify goals and values. They may also benefit from interactions with other chronic pain patients.

7.5.3. Assessment of Potential Risks and Benefits

The risks associated with this study are minimal. Study team will monitor for any complaints related to survey discomfort and breaches in confidentiality.

8. Supporting Documentation and Operational Considerations

8.1. Regulatory, Ethical, and Study Oversight Considerations

8.1.1. Informed Consent Process

8.1.1.1. Consent/assent and Other Informational Documents Provided to participants

Consent forms describing in detail the study intervention, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting study.

8.1.1.2. Consent Procedures and Documentation

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Consent forms will be Institutional Review Board (IRB)-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate.

The participant will electronically sign the informed consent document prior to any procedures being done specifically for the study. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be available to the participants. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

8.1.2. Study Discontinuation and Closure

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants and investigator. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the sponsor and IRB.

8.1.3. Confidentiality and Privacy

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and their interventions. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval.

All research activities will be conducted in as private a setting as possible. At the beginning of group sessions, ground rules will be shared with the participants. These rules will encourage participants to maintain confidentiality, privacy and dignity of the members in the group.

Representatives of the Institutional Review Board (IRB) or regulatory agencies may inspect all documents and records required to be maintained by the investigator.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at the B&PC Research Center. This may include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by B&PC Research Center staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived here.

8.1.4. Future Use of Data

Data collected for this study will be analyzed and stored at the B&PC Research Center. After the study is completed, the de-identified, archived data will be transmitted to and stored at the B&PC Research Center, for use by other researchers including those outside of the study.

When the study is completed, access to study data and/or samples will be provided through the B&PC Research Center.

8.1.5. Key Roles and Study Governance

Principal Investigator	**Principal Investigator**	**Principal Investigator**
Hannah Smotrich	Stephanie Tharp	Afton Hassett
STAMPS Faculty	STAMPS Faculty	Back & Pain Center
734-763-5226	734-763-5226	734-763-5226
smotrich@umich.edu	smtharp@umich.edu	afton@med.umich.edu

8.1.6. Safety Oversight

Safety oversight will be under the direction of a designated study monitor, designated from the study team. They will be responsible for reviewing regulatory compliance and ensuring participant and data safety. The study monitor will review the study on an annual basis and complete documentation.

8.1.7. Clinical Monitoring

Clinical site monitoring is conducted to ensure that the rights and well-being of trial participants are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with International Conference on Harmonization Good Clinical Practice (ICH GCP), and with applicable regulatory requirement(s).

A study monitor will conduct an audit on an annual basis by reviewing 10% of the records randomly. Errors and discrepancies will be documented and reviewed with the study team.

8.1.8. Quality Assurance and Quality Control

Our clinical site will perform internal quality management of study conduct, and data documentation and completion.

Quality control (QC) procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/resolution.

Following written Standard Operating Procedures (SOPs), the monitors will verify that the clinical trial is conducted and data are generated and biological specimens are collected, documented (recorded), and reported in compliance with the protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), and applicable regulatory requirements (e.g., Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP)).

The investigational site will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by local and regulatory authorities.

8.1.9. Data Handling and Record Keeping

8.1.9.1. Data Collection and Management Responsibilities

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All data will be recorded in the electronic case report form (eCRF) derived from source documents should be consistent with the data recorded on the source documents.

Clinical data (including adverse events (AEs), concomitant medications, and expected adverse events data will be entered into REDCap, a 21 CFR Part 11-compliant data capture system provided by the University of Michigan. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate.

8.1.9.2. Study Records Retention

Study documents should be retained for a minimum of 2 years have elapsed since the formal discontinuation of clinical development of the study intervention. These documents should be retained for a longer period, however, if required by local regulations. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained

8.1.10. Protocol Deviations

It is the responsibility of the site investigator to use continuous vigilance to identify and report deviations as described in **Error! Reference source not found.**. Protocol deviations must be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements.

8.1.11. Conflict of Interest Policy

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. All study group members will be asked to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

8.2. Additional Considerations

N/A

8.3. **Abbreviations**

AE	Adverse Event
ANCOVA	Analysis of Covariance
B&PC	Back & Pain Center
CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
CMP	Clinical Monitoring Plan
COC	Certificate of Confidentiality
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
DRE	Disease-Related Event
EC	Ethics Committee
eCRF	Electronic Case Report Forms
FFR	Federal Financial Report
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
GWAS	Genome-Wide Association Studies
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICH	International Conference on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IDE	Investigational Device Exemption
IND	Investigational New Drug Application
IRB	Institutional Review Board
ISM	Independent Safety Monitor
ISO	International Organization for Standardization
ITT	Intention-To-Treat
LSMEANS	Least-squares Means
MedDRA	Medical Dictionary for Regulatory Activities
MSDS	Material Safety Data Sheet
NCT	National Clinical Trial
NIH	National Institutes of Health
NIH IC	NIH Institute or Center
OHRP	Office for Human Research Protections
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SMC	Safety Monitoring Committee
SOA	Schedule of Activities
SOC	System Organ Class
SOP	Standard Operating Procedure
UaP	Unanticipated Problem

8.4. Protocol Amendment History

The table below is intended to capture changes of IRB-approved versions of the protocol, including a description of the change and rationale.

Version	Date	Description of Change	Brief Rationale

8.5. Appendix A: Intervention Documents

8.6. References

1. 'Unrelieved Pain is a Major Global Healthcare Problem.' International Association for the Study of Pain. Accessed January 4, 2020. http://www.iasp-pain.org/ (pdf, p.1).