# Parker UniversityResearch Protocol Template

*{Replace with your study title.****Item 1:*** *Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym.*

*IRB application #1}*

# *PREFACE*

*The goal of this template is to provide a general format applicable to all research projects. Instructions and explanatory text are indicated by italics, please replace these sections in your protocol with appropriate text. Section headings and template text formatted in regular type should be included in your protocol document as provided in the template.*

*Blue italics represents items from the SPIRIT checklist, if examples or more information needed see the SPIRIT Checklist:* [*https://www.spirit-statement.org/*](https://www.spirit-statement.org/)

*Green italics states where on the Parker IRB application this information will be shared. NOTE: The audience and purposes of the IRB application and this document are different, ensure that the language is appropriate for each.*

**SUPPORTED BY:**

*Include application or grant number(s) when available.*

***Item 4:*** *Sources and types of financial, material, and other support.*

*IRB application #5*

**PARTICIPATING STUDY SITES:**

*List the name and address of each study site, including investigator (contact), telephone and e-mail address.*

*IRB application #6*

**TRIAL REGISTRATION INFORMATION:**

***Item 2a:*** *Trial identifier and registry name. If not yet registered, name of intended registry.*

**ETHICS APPROVAL(s):**

***Item 24:*** *Plans for seeking research ethics committee/institutional review board (REC/IRB) approval.*

# STUDY PERSONAL - AUTHORSHIP CONSIDERATIONS

*{Make sure personnel here match that listed in the IRB application #3)****Item 5a:*** *Names, affiliations, and roles of protocol contributors.*

***Item 31b:*** *Authorship eligibility guidelines and any intended use of professional writers.*

|  |  |  |
| --- | --- | --- |
| ICMJE recommends that authorship be based on the following 4 criteria: | **Proposed Study Personnel\* Involvement & Affiliation(s)** | **Email** |
| **1.** | Substantial contributions to the conception or design of the work; OR |  |  |
|  | the acquisition of data for the work; OR |  |  |
|  | the analysis of data for the work; OR |  |  |
|  | the interpretation of data for the work. |  |  |
| **2.** | Drafting the work; OR |  |  |
|  | revising it critically for important intellectual content. |  |  |
| **3.** | Final approval of the version to be published. |  |  |
| **4.** | Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. |  |  |

\* Study personnel must have a thorough understanding of their portion of the study (and be aware of all portions). Not all study personnel are expected/required to be authors. If study personnel do not meet all criteria, they should be invited to be acknowledged in any scientific outputs.

In order to be listed as an author on a poster/presentation/manuscript, an individual must have contributed to all four categories. Authors are expected to be able to answer/support any questions related to the research question, design, and results.

NOTE: Final order of authorship is at the discretion of the senior author and will be determined by individual contributions relating to the study idea, design and data collection, writing of the manuscript, as well as general volume of work contributed and used.

# 1. STUDY OBJECTIVES

*IRB application #8a*

***Item 7:*** *Specific objectives or hypotheses.*

## 1.1 Primary Objective

The primary objective should be specific and include population / intervention / comparison / outcome / timeline (as applicable). The hypothesis needs to be stated in quantifiable terms.

## 1.2 Secondary Objectives

Secondary objectives may or may not be hypothesis-driven, may include secondary

outcomes, and may include more general non-experimental objectives (e.g., to develop a registry, to collect natural history data). State the hypothesis when applicable.

# 2. INTRODUCTION / BACKGROUND / SIGNIFICANCE

Introduce the study, capture the reader’s attention and prepare them for the body of the introduction / background.

* Thoroughly describe what is known about the condition and/or intervention currently in the literature.
* Thoroughly describe the gaps that are currently in literature and the impact this has on society/individuals.
* Thoroughly describe the significance of this study and how it will answer the intended research question. Include a thorough explanation of the **need**, **relevance,** and **priority** for the study. (NOTE: priority explains why this study is important to do versus all the other studies that also need to be done.)

\*\*\*In each part, ensure the paragraphs exhibit a logical progression of sophisticated ideas and empirical research that supports the focus of the study.

*IRB application #8b*

***Item 6a:*** *Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention.*

***Item 6b:*** *Explanation for choice of comparators.*

# 3. STUDY PROCEDURES

## 3.1 Study Design

Briefly describe the study design (e.g., parallel groups, crossover, immediate versus deferred intervention, factorial, large simple trial, equivalency or non-inferiority trial). If applicable, describe why certain design features were chosen (e.g., for a crossover trial, why a specific length of washout period was chosen). Indicate, in general terms, how the design will answer the question posed by the study.

It is recommended to include a study flow diagram, which can include added visual explanation for any design complexities. Example:

## Enrollment

Assessed for eligibility

Excluded

Allocated to comparison

## Allocation

Allocated to intervention

## Follow-Up

Study Completion

Study Completion

*IRB application #8c*

**Item 8:** Description of trial design including type of trial (e.g., parallel group, crossover, factorial, single group), allocation ratio, and framework (e.g., superiority, equivalence, non-inferiority, exploratory).

## 3.2 Recruitment

 *Give a detailed methodology for how you will recruit candidates for the study. Recruitment is the most common reason that studies are not successful. Include details of prior networking / projects that suggest this recruitment plan will be successful. Detail any personal or professional connections that will aid you in successfully reaching your recruitment goals. If possible, include contingency plans (e.g., changing eligibility criterion or other places to network/recruit).*

* *If you are going to use flyers, include a reference to them here, as well as the actual flyer / informational items as appendices in the protocol.*

*IRB application #12a*

***Item 15:*** *Strategies for achieving adequate participant enrollment to reach target sample size.*

## 3.3 Randomization

Describe the procedures for assigning participants their respective groups:

* How will the randomization codes be developed and what are the plans for the maintenance of trial randomization codes.
* If the randomization will be stratified, identify what factors (if any) will be used and provide justification. Specify the time window for (a) randomization relative to completion of screening and at baseline as well as (b) initiation of study intervention relative to randomization.

*IRB application #8d*

**Item 16a:** Method of generating the allocation sequence (e.g., computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (e.g., blocking) should be provided in a separate document that is unavailable to those who enroll participants or assign interventions.

**Item 16b:** Mechanism of implementing the allocation sequence (e.g., central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned.

**Item 16c:** Who will generate the allocation sequence, who will enroll participants, and who will assign participants to interventions.

## 3.4  Participant Timeline and Data Collection Methods

Describe all study interactions and indicate treatment and assessments for each of these. Include allowable time window in which evaluations may take place, e.g., study visits must be performed on the weeks ± X days. The evaluation time window should be as narrow as technically feasible.

This section should include a table with a schedule of evaluations that includes all study evaluations, such as eligibility criteria, baseline evaluations / characteristics / demographics (confounding factors), and outcome measures. The evaluations should reflect the protocol and should be arranged for clearest presentation. Include data collection forms in the appendix of this document.

Describe each assessment to be performed at the participant’s final visit and/or follow-up visits, as well as any other additional procedures to be done, such as an exit interview or debrief interview. Consider specifying evaluations needed for participants who discontinue study intervention early, specify potential reasons for early termination, and specify any requirements (e.g., related to monitoring) for follow-up on participants once they have stopped using the study intervention.

*IRB application #8e*

**Item 13:** Time schedule of enrollment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure 1).

**Item 18a:** Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (e.g., duplicate measurements, training of assessors) and a description of study instruments (e.g., questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol.

## Example of a table with a schedule of evaluations

| **Assessment** | **Screening Visit** | **Baseline, Enrollment, Randomization, Treatment Visit 1 (Day 0)** | **Treatment Visit 2 (W2)** | **Treatment Visit 3 (W5)** | **Treatment Visit 4 (W8)** | **Follow-up: Final Visit****(W10)** |
| --- | --- | --- | --- | --- | --- | --- |
| **Informed Consent Form** | **X** |  |  |  |  |  |
| **Demographics** | **X** |  |  |  |  | **X** |
| **MRI / Xray** | **X** |  |  |  |  | **X** |
| **Medical History**  | **X** |  |  |  |  |  |
| **Physical Examination** | **X** | **X** | **X** |  | **X** | **X** |
| **Current Medications** | **X** | **X** |  |  |  |  |
| **NRS** | **X** | **X** | **X** | **X** |  | **X** |
| **Disability Questionnaire** | **X** | **X** | **X** | **X** |  | **X** |
| **Adverse Events**  |  | **X** | **X** | **X** | **X** | **X** |

## 3.5 Blinding

Describe blinding and unblinding justifications of all key roles (participant, provider, investigators, outcome assessor, biostatistician). Address the following points:

* Procedure for retaining the blinded intervention (including specific procedures for protecting the person who is blinded, should the data collected in the study offer evidence of a participant’s assignment to a particular study arm).
* Individual authorized to break the blind and/or the circumstance/procedures for the blinding to be broken, if applicable.
* Avoid out-dated terms such as ‘single’ or ‘double’-blinded

*IRB application #8f*

**Item 17a:** Who will be blinded after assignment to interventions (e.g., trial participants, care providers, outcome assessors, data analysts), and how.

**Item 17b:** If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant’s allocated intervention during the trial.

## 3.6 Training

Describe the types of and mechanisms for the training of staff for the study. Example:

Full team trainings on study protocol will occur one month prior to the start of study enrollment. In-person team meetings will occur bi-weekly with review of study protocols.

# 4. SELECTION OF PARTICIPANTS

One key component of a successful research study is the selection and enrollment of participants who are representative of the populations or characteristics under investigation. This section must explicitly define the study population and how they will be assessed for eligibility.

Include a table that describes the criterion, a rationale for this criterion and what will assess the criteria. See the example below:

## Example of a table with eligibility criteria described

|  |  |  |
| --- | --- | --- |
| **Inclusion Criteria** | **Rationale** | **Assessed** |
| Age 18-65 years, inclusive | Individuals >65 years are not as likely to tolerate the biomechanical tests and experience altered sensorimotor function. Children/Young adults not considered for study. | Phone Screen, Study Coordinator |
| Signed Informed Consent Document | Research policy | Baseline Visit, Study Coordinator |
| Numerical Pain Rating Scale of >4 at PS & BL1 | Low back pain with enough severity to demonstrate clinically meaningful improvements | Phone Screen & Baseline Visit, Study Coordinator |
| **Exclusion Criteria** | **Rationale** | **Source** |
| Inability to read or verbally comprehend English | Difficult to ensure full consent | Phone Screen & Baseline Visit, Study Coordinator |
| Beck Depression Index > 29 | Significances advance depression, this may interfere with the participants ability to comply with study protocol, data collection, and/or confound outcome/condition. | Baseline Visit, Study Coordinator |

*IRB application #9*

**Item 10:** Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (e.g., surgeons, psychotherapists).

# 5. STUDY INTERVENTIONS: Intervention(s) / Comparison(s)

Describe how each study intervention / comparison group(s) will be administered and the schedule of delivery. This should be written **explicitly**, ensure that the interventions are reproduceable by anyone who reads the guidelines. Indicate the setting the intervention will be administered in (e.g., outpatient, exercise laboratory, intensive care unit) and planned treatment modifications (e.g. dose escalation), if relevant. State guidelines for use of appropriate supportive care or treatments. Include instructions for modifications to the study interventions, if appropriate and clearly explain modification of dose due to adverse event or any other reason.

*IRB application #10*

**Item 11a:** Interventions for each group with sufficient detail to allow replication, including how and when they will be administered.

# 6. OUTCOME MEASURE(S) / STATISTICAL CONSIDERATIONS

## 6.1 Description of Outcomes

For each outcome measure for this study, include what is known about the property measurements (validity / reliability) and clinically meaningful differences. Describe who may be masked to the participant’s intervention group assignment during the outcome assessment.

**Item 12:** Primary, secondary, and other outcomes, including the specific measurement variable (e.g., systolic blood pressure), analysis metric (e.g., change from baseline, final value, time to event), method of aggregation (e.g., median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended.

Example:

The primary outcome is the Numeric Rating Scale (NRS) for average pain intensity during the past week. The NRS has excellent metric properties, is commonly used in RCTs studying LBP [Childs et al., 2005; van der Roer et al., 2006], and has been demonstrated as a valid and reliable measure [Jensen et al., 2001]. Participants are asked to rate their average level of LBP during the past week on an ordinal 11-box scale (0 = no LBP; 10 = worst possible LBP).

## 6.2 Sample Size

Describe sample size calculation, including software program used, and effect size with respect to power. Specify the test statistic; Type I and Type II error rates; assumed event rate for dichotomous outcome (mean and/or variance for continuous outcome) for each study arm (include the references from which this information was retrieved); assumed rates of drop-out, withdrawal, cross-over to other study arms, and missing data, etc..

*IRB application #8h*

**Item 14:** Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations.

## 6.3 Data Analyses

Describe both the descriptive and inferential statistical methods that will be used to analyze the outcomes and other study data, include whether an ITT (intent to treat) and per protocol analysis is intended (and if/how missing data will be handled). Specify any confounding variables for which it is anticipated adjustment will be made. Include any draft tables of data analysis in the appendix of this document.

*IRB application #8g*

**Item 20a:** Statistical methods for analyzing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol.

**Item 20b**: Methods for any additional analyzes (e.g., subgroup and adjusted analyzes).

**Item 20c**: Definition of analysis population relating to protocol non-adherence (e.g., as randomized analysis), and any statistical methods to handle missing data (e.g., multiple imputation).

# 7. ETHICAL CONSIDERATIONS

## 7.1 Consenting Process

*This section describes the procedures for obtaining and documenting informed consent of study participants in detail, including location, personnel involved, and how a copy of the document will be given to each participant. Include and reference the study’s consent form in the appendix of this document.*

* *If applicable, describe provisions for special populations, e.g., non-English speakers, children (include details of assent), illiterate or non-writing individuals, vulnerable populations. Example Text:*
* *For participants who cannot consent for themselves, such as those with a legal guardian (e.g., person with power of attorney), the legal guardian must sign the consent form.*

*IRB application #12b*

***Item 26a:*** *Who will obtain informed consent or assent from potential trial participants or authorized surrogates, and how (see Item 32).*

## 7.2 Participant Confidentiality

Include procedures for maintaining participant’s confidentiality according to the Health Insurance Portability and Accountability Act (HIPAA), any special data security requirements, and record retention per the sponsor’s requirements. **Do not simply copy the below paragraph if it is not how you will be maintaining participant confidentiality.**

*IRB application #11b*

**Item 27:** How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial.

Example:

To maintain participants’ confidentiality, all data collected will be stored at Parker on a secured encrypted server to which only specified personnel will have access. Any reports needed to facilitate efficient project management will be built in the REDCap report modules. The Windows Server environment is password protected with Microsoft Windows Active Directory and meets HIPAA standards. The principal investigator will generate, transfer, and store datasets on secured servers as requested by the team. Copies of final datasets, tables, programs, and documentation will be securely stored on site.

A unique system study ID will be assigned during initial consent on REDCap. The study ID is not linked or derived from any participant related information. Identifiable data will be used for contact purposes only during the study participation phases. After the participant has completed the study all individually-identifiable information will be removed from study related data sources. Only the study ID will remain as an identifier for data management and analysis purposes. Information will not be released without written permission of the participant, except as necessary for monitoring by IRB. All study staff will be trained in confidentiality procedures.

## 7.3 Safety Assessments

Participant safety should be monitored once an individual is enrolled in the study. To assure comprehensive review of potential safety events, include a list of expected adverse experiences for each study intervention, criteria for management and modification of the study intervention regimen or participant assessments if an adverse event occurs.

*IRB application #12e*

**Item 22:** Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct.

### 7.3.1 Adverse Events and Serious Adverse Events Definitions

Provide definitions for adverse events (AEs) and serious adverse events (SAEs). Example:

An **adverse event (AE)** is generally defined as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during the study, having been absent at baseline, or if present at baseline, appears to worsen. Adverse events must be recorded regardless of their relationship to the study intervention.

A **serious adverse event (SAE)** is generally defined as any untoward medical occurrence that results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, or results in persistent or significant disability/incapacity, or is a congenital anomaly.

### 7.3.2 Unexpected Study Events

Provide definitions for unexpected study events. Example:

Unexpected study events will be classified into three categories: protocol deviations, protocol violations, and unanticipated events.

**Protocol deviations** will be defined as any variance in the approved study protocol, criteria or procedure that does not affect the participant’s safety, rights, welfare or the integrity of the study and its resultant data.

**Protocol violations** are deviations that increase the risk or decrease the benefit and/or affect the participant’s rights, safety, welfare and/or integrity of the resultant data.

**Unanticipated Events** are deviations that do not meet the above definitions but may affect the rights, safety, welfare and/or integrity of the resultant data.

## 7.4 Reporting Procedures

All clinical trials must have a safety reporting system in place. Include details of the reporting procedures and time lines, including the individual responsible for each step (e.g., study coordinator, investigator.), how decisions will be made regarding determining relatedness and severity, which forms should be completed, where to send specific information, and how reports will be distributed and what follow-up is required. Example:

Inquiry about adverse events will be done at all study visits by the study coordinator asking “Did you experience any discomfort or unpleasant reaction after any of your {intervention / comparison}?” A “yes” response will be followed by completion of the Parker University Clinical Trial Patient Safety Monitoring form, which requires a description of the event (e.g., increased pain, stiffness, muscle weakness, headache). Severity of event will be rated by checking one of the following categorical responses: Symptoms did NOT require changing or modifying regular activities (mild); Symptoms required modifying regular activities or for which treatment is needed (moderate); Symptoms required bed rest, lost work, or prevented you from regular activities (severe); Symptoms were life-threatening or required in-patient hospitalization (severe). Duration of symptoms will also be recorded (less than 24 hrs; 24-48 hrs; 48hrs-1 week; 1-4 weeks; >4 weeks). The relationship to the study intervention, expectedness, and outcome of the adverse event will be assessed by the Project Manager with the treating clinician assisting, if necessary.

Participants will also be instructed to contact study staff if they experience a change in health status or significant pain, discomfort or distress regardless of whether or not they believe it may be associated with treatment including after final treatment. Participants are also asked to inform the Project Manager of any unplanned emergency room or hospitalizations for either LBP or mental health issues.

All study events will be reviewed by the lead/site project investigator(s). IRB submission of study events will be dictated by the reporting requirements for the study IRB. Specifically, all SAEs and Unexpected Study Events will be reported to Parker’s IRB within 5 business days of becoming aware of the event. Events not meeting these criteria for immediate reporting will be submitted to the IRB in summary format during the annual continuing review. The study’s project manager/study coordinator will follow-up with the participant until the event is completely resolved or determined unnecessary to follow-up by the IRB.

# REFERENCES

Provide the citations for all referenced in the text of the protocol.

# SUPPLEMENTS/APPENDICES

Examples:

Informed Consent Document
Item 32: Model consent form and other related documentation given to participants and authorized surrogates.

Data Collection Forms/Instruments

Draft of Intended Results Table

Letters of Support

Recruitment Flyers / Informational Sheets

# SPIRIT Items not included in this protocol:

***Item 2b****: All items from the World Health Organization Trial Registration Data Set.*

***Item 5b:*** *Name and contact information for the trial sponsor.*

***Item 5c****: Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities.*

***Item 5d:*** *Composition, roles, and responsibilities of the coordinating center, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for Data Monitoring Committee).*

***Item 9:*** *Description of study settings (e.g., community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained.*

***Item 11b:*** *Criteria for discontinuing or modifying allocated interventions for a given trial participant (e.g., drug dose change in response to harms, participant request, or improving/worsening disease).*

***Item 11c:*** *Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (e.g., drug tablet return; laboratory tests).*

***Item 11d:*** *Relevant concomitant care and interventions that are permitted or prohibited during the trial.*

***Item 18b:*** *Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols.*

***Item 19:*** *Plans for data entry, coding, security, and storage, including any related processes to promote data quality (e.g., double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol.*

***Item 21a:*** *Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed.*

***Item 21b:*** *Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial.*

***Item 23:*** *Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor.*

***Item 25:*** *Plans for communicating important protocol modifications (e.g., changes to eligibility criteria, outcomes, analyses) to relevant parties (e.g., investigators, REC/IRBs, trial participants, trial registries, journals, regulators).*

***Item 26b:*** *Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable.*

***Item 28:*** *Financial and other competing interests for principal investigators for the overall trial and each study site.*

***Item 29:*** *Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators.*

***Item 30:*** *Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation.*

***Item 31a:*** *Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (e.g., via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions.*

***Item 31c:*** *Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code.*

***Item 33:*** *Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable.*