# National Institute of Arthritis and Musculoskeletal and Skin Diseases

# Template and Guidelines for Developing a Single-Site Manual of Operations and Procedures (MOOP)

***October 2017***

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## APPENDICES

## ABBREVIATION GLOSSARY

***Case Report Form (CRF) –*** A printed, optical, or electronic (eCRF) document designed to record information about study participants.

***Clinical Research or Study Coordinator (CRC) –*** An individual that handles the administrative and day-to-day responsibilities of a clinical trial. This person may collect or review data before it is entered in the study database.

***Code of Federal Regulations (CFR) –*** An annual compilation of rules and regulations published in the Federal Register by the executive departments and agencies of the Federal Government.

***Coordinating Center (CC) –*** A group organized to coordinate the planning and operational aspects of a multi-center clinical trial. CCs may also be referred to as Data Coordinating Centers (DCCs) or Data Management Centers (DMCs).

***Conflict of Interest (COI) –*** A conflict of interest occurs when individuals involved with the conduct, reporting, oversight, or review of research also have financial or other interests that may be affected by the results of the research.

***Data and Safety Monitoring Board (DSMB) –*** An oversight body that is independent of the study investigators, and is appointed by the NIAMS to monitor participant safety and data quality, and to assess clinical trial progress.

***Food and Drug Administration (FDA) –*** An agency within the U.S. Department of Health and Human Services (DHHS), responsible for protecting public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, nation's food supply, cosmetics, and products that emit radiation.

***Good Clinical Practice (GCP) –*** Section 2 from the International Council for Harmonisation provides guidance for good design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials to ensure data and results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

***Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule –*** Public Law 104-191 provides for the protection of personal health information. The Privacy Rule, Title II of the Act, regulates the way certain health care groups, organizations, or businesses, called covered entities under the Rule, use and disclose individually identifiable health information known as protected health information (PHI). Title II also establishes that covered entities ensure the security and privacy of PHI.

***Institutional Review Board (IRB)/Independent Ethics Committee (IEC) –*** An independent body consisting of medical, scientific, and non-scientific members whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trials, protocols and amendments, and of the methods and materials to be used to obtain and document the informed consent of trial participants.

***International Conference on Harmonisation (ICH) –*** An international collaboration between the United States, the European Union and Japan to harmonize the testing requirements of pharmaceutical products intended for human use. ICH's mission is to achieve greater harmonisation worldwide to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner. Harmonisation is achieved through the development of ICH Guidelines via a process of scientific consensus with regulatory and industry experts working side-by-side.

***Investigational New Drug Application (IND)/Investigational Device Exemptions (IDE) –*** An IND is the means through which the Food and Drug Administration (FDA) grants the sponsor permission to administer an investigational drug or biological product to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biological product that is not the subject of an approved New Drug Application or Biologics/Product License Application (21 CFR 312). An IDE allows the investigational device to be used in a clinical trial to collect safety and effectiveness data for human use (21 CFR 812).

***Manual of Operating Procedures (MOOP)/Manual of Procedures (MOP) –*** A "cookbook" that translates the protocol into a set of operational procedures to guide study conduct. A MOOP/MOP is developed to facilitate consistency in protocol implementation and data collection across study participants and clinical sites.

***Not Applicable (NA) –***When recording data on a study form, if the information is not applicable, then the acronym NA should be used to fill out the field.

***Not Available (NAV) –*** When recording data on a study form, if the information is not available, then the acronym NAV should be used to fill out the field.

***Not Done (ND) –*** When recording data on a study form, if the evaluation required for a field is not done, then the acronym ND should be used to fill out the field.

***Observational Study Monitoring Boards (OSMBs) –*** A body independent of the investigators that is appointed by the NIAMS to provide ongoing review for an observational study. The OSMB closely monitors data acquisition for comprehensiveness, accuracy, and timeliness as well as and monitoring participant safety and confidentiality.

***Office for Human Research Protection (OHRP) –*** A federal government agency within the Department of Health and Human Services (DHHS) charged with the protection of

human subjects participating in government-supported research. The OHRP issues assurances to institutions reviewing human subjects research and oversees compliance of regulatory guidelines by research institutions.

***Principal Investigator (PI) –*** The individual with primary responsibility for achieving the technical success of the project, while also complying with the financial rules and requirements, administrative policies, and regulations associated with a grant or award. Although Principal Investigators may have administrative staff to assist them with the management of project funds, the ultimate responsibility for the management of the research project rests with the Principal Investigator.

***Quality Control (QC) –*** The internal operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of trial related activities have been fulfilled (e.g., data and form checks, monitoring by study staff, routine reports, correction actions, etc.).

***Safety Monitoring Plan (SMP) –*** A plan that outlines the oversight of a clinical trial.

***Safety Officer (SO) -*** The Safety Officer is an independent individual, usually a clinician, who performs data and safety monitoring activities in low-risk, single-site clinical studies. The Safety Officer advises the NIAMS Program Director regarding participant safety, scientific integrity and ethical conduct of a study.

***Standard Operating Procedure (SOPs) –*** Detailed written instructions to achieve uniformity of the performance of a specific function across studies and patients at an individual site.

***Unknown (UNK)-*** When recording data on a study form, if the information is unknown, then the abbreviation UNK should be used to fill out the field.

## INTRODUCTION

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH) must ensure compliance with Federal laws and regulations, including procedures and policies to protect the safety of all participants in the clinical studies it supports. In preparing to implement a study, the Principal Investigator must be aware of the terms of the award outlined in their Notice of Grant Award (NGA), with respect to required reporting, data and safety monitoring oversight, and Institutional Review Board (IRB) approval.

The purpose of this document is to assist investigators of single-site studies in the preparation of a study Manual of Operating Procedures (MOOP), by providing them with a template and guideline. A single-site study is defined as involving only one clinic (i.e., performance site) and a center (e.g., data coordinating center) to receive and process data. The performance site and coordinating center may or may not be in the same location. The role of the MOOP is to facilitate consistency in study implementation and data collection across study visits and participants. Use of the MOOP increases the likelihood that the results of the study will be scientifically credible, that participant safety will be protected, and scientific integrity will be closely monitored.

The NIAMS website lists many links and references to helpful policies, procedures and templates related to clinical research (see https://www.niams.nih.gov/). All staff members participating in the conduct of this study at participating institutions should have ready access to the MOOP and be familiar with its contents.

## HOW TO USE THIS DOCUMENT

This is a template and guidance document to be used by investigators developing a MOOP for clinical studies supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). Please read this document to understand how to create your study specific MOOP. Note that the contents provided in **this document are informational, and include examples of how to develop your study-specific MOOP**. If a particular section is not relevant to your particular study, there is no need to include it. Refer to the MOOP Outline and Guide on page 9 for the elements that are expected to be included in your study specific MOOP.

The sample texts are provided as examples to help you develop your MOOP content. Upon completion of each section of your MOOP, please refer to the checklist to ensure you have captured all the relevant information for that specific section.

Key

- Sample text is in ***bold italics***
- Checklist samples are in **text boxes**

**Note: Please do not use the text verbatim.**

## OVERVIEW

A MOOP is for clinical interventional trials (e.g., drug, surgery, behavioral, device, etc.). The MOOP transforms the study protocol into a handbook for study staff. Its purpose is to provide the operational detail to ensure that study procedures are carried out consistently. The study team (investigators, coordinators, statisticians, etc.) develops the MOOP and submits it to the NIAMS for approval before the study can commence.

MOOP development requires complete versions of a final protocol, study forms (often called case report forms (CRFs)), Investigator Brochure (IB) or Device Manual, if applicable, and Informed Consent Form (ICF).

The MOOP is a dynamic document that must be updated throughout the study to reflect any protocol or ICF amendments, as well as the refinement of the CRFs and study procedures. The MOOP should be maintained in a format that allows it to be easily referenced and updated, such as a three-hole binder or electronic format. Each page of paper copy of the MOOP should have the version number and date; electronic versions of the MOOP should have consistent naming nomenclature that includes version dates. Older versions of paper and/or electronic versions must be archived. Once approval to begin the study is received, any changes to the MOOP, including the new version number and date, should be submitted to the NIAMS with track changes for easy reference for review and approval before implementation of any modifications.

The MOOP sections outlined below and described in detail in subsequent sections of this document are a guideline rather than a prescription and should be adapted to each study's specific needs. If a section is not relevant to the study (e.g., randomization in a study with no randomization), it obviously should not be included in the MOOP.

**MOOP OUTLINE AND GUIDE**

**1.0 Introduction**

The MOOP submitted to the NIAMS should include all the elements listed below, if relevant. A copy of the study protocol should be included as appendix A. For additional information on how to use the NIH-FDA approved protocol template for FDA regulated Phase 2 or 3 studies http://osp.od.nih.gov/office-clinical-research-and-bioethics-policy/clinical-research-policy/clinical-trials. Additionally, there is an electronic protocol writing tool that aims to facilitate the development of phase 2 and 3 clinical trial protocols that require a Food and Drug Administration (FDA) Investigational New Drug (IND) or Investigational Device Exemption (IDE) Application https://e-protocol.od.nih.gov/#/home.

a. Study Overview
b. Study Flow Diagram
c. Staff Roster, Organization, and Responsibilities
d. Recruitment and Retention Plan
e. Screening and Eligibility Criteria
f. Informed Consent and HIPAA Process
g. Study Intervention
h. Randomization
i. Masking and Unmasking
j. Participant Evaluations and Follow-up
k. Concomitant Medications
l. Safety Reporting
m. Data and Safety Monitoring Activities
n. Study Compliance
o. Data Collection and Study Forms
p. Data Management
q. Reports
r. Study Completion and Close-Out Procedures
s. Policies
t. MOOP Maintenance

## 2.0 Study Overview

This section of the MOOP should provide a brief (approximately 500-750 words) overview of the study.

***Sample Text:***
***Title: Effects of Instructor-Led Exercises on Improved Osteoporosis Outcomes***

***This is a randomized double-blind, placebo-controlled trial with individuals aged 18-90 with osteoporosis. This study investigates the effect(s) of an experimental series of exercises on improved bone density outcomes. This study will enroll 200 participants and have 20 visits over a one year period. Data collection will occur at each visit, with baseline data collected at the initial visit. A 3-month follow-up will be conducted over the phone from the date of the final visit.***

**Checklist:**

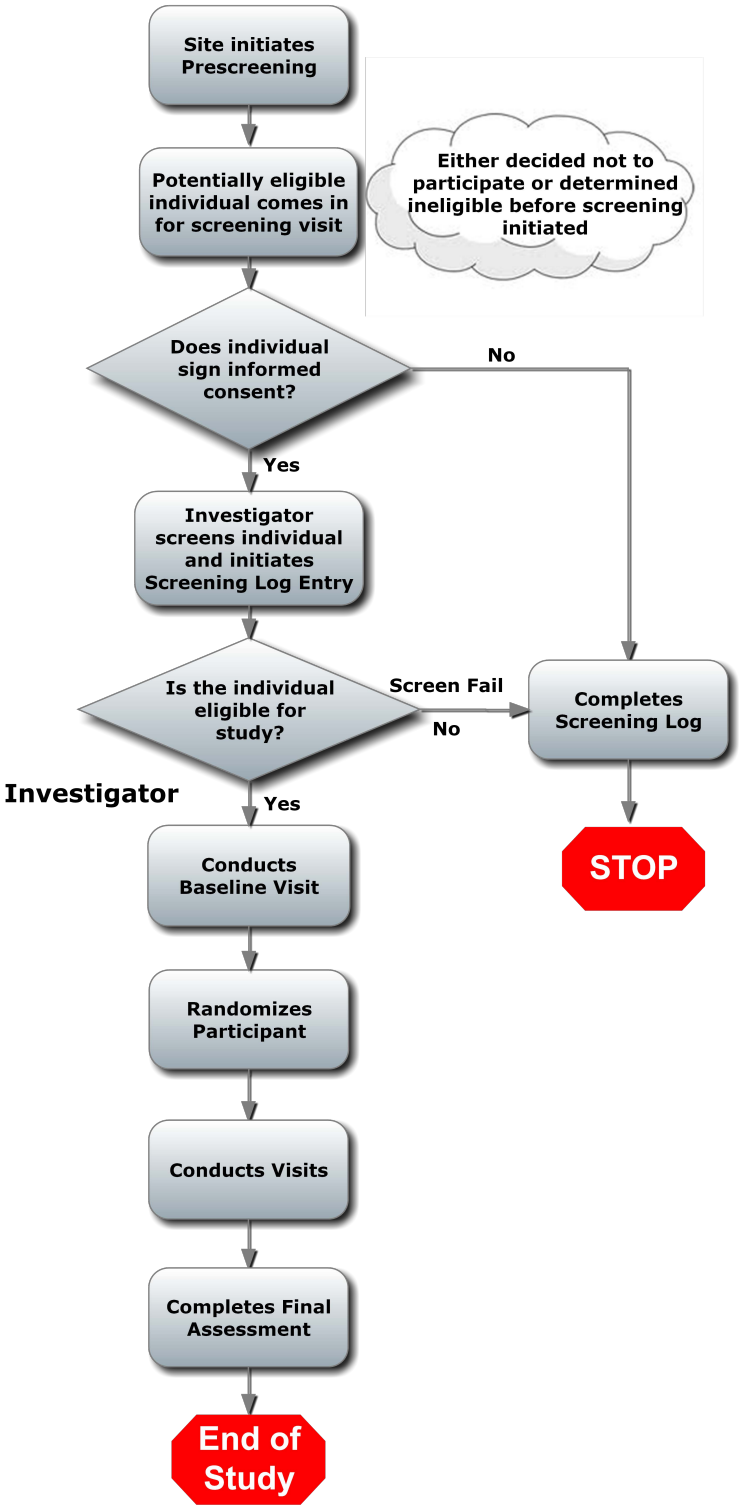
- **Study Type**
  - **Number of Arms**
- **Patient Demographics**
- **Patient Condition**
- **Study n**
- **Study Duration**
- **Study Time Points**
- **Study Design**

## 3.0 Study Flow Diagram

This section should include the overview of the study processes in a flow diagram. For example, Figure 1 below, describes each of the study's major steps. It should be uniquely tailored to the study and should be helpful in describing the study to new staff members. For each step, be sure to denote which staff member(s) are taking action.

**FIGURE 1:**

***SAMPLE STUDY DIAGRAM***



## 4.0 Staff Roster, Organization and Responsibilities

This section should provide a roster of the study staff and a brief description of their roles as well as an organization chart.

For example, in a single-site study, the clinical site staff may perform the duties of both a center (e.g., data coordinating center) and the clinic (i.e., performance site), or there could be a separate center handling the data coordinating activities.

***Sample Text:***
***This table describes the study's organizational scheme and provides a roster of the members and roles of the study team. For each study team member, a mailing address, two phone numbers, email address, and study role are provided.***

## ***Table 1: Sample Staff Roster***

| Name | Address | Phone | Email | Role | Responsibilities |
|---|---|---|---|---|---|
| *John Brown* | *City Hospital<br>Research Department<br>123 Brown Street<br>Suite 535 B<br>New York, NY 10000* | *Office:<br>(212) 123-4567<br><br>Cell:<br>(212) 508-5518* | *jbrown@univ.edu* | *Principal investigator* | • *Identification, recruitment, screening, and enrollment of participants*<br>• *Reporting and monitoring of adverse events*<br>• *Obtaining informed consent from each participant*<br>• *Randomization of participants*<br>• *Compliance with and accountability of study intervention administration*<br>• *Submitting documents to regulatory bodies (i.e., IRB or FDA*<br>• *Quality control procedures*<br>• *Ensuring compliance with human subjects regulations and policies* |
| *Mary Smith* | *City Hospital<br>Research Department<br>123 Brown Street<br>Suite 400<br>New York, NY 10000* | *Office:<br>(212) 123-4568<br><br>Cell:<br>(212) 123- 5761* | *Msmith@univ.edu* | *Study Coordinator* | • *Obtaining informed consent from each participant*<br>• *Collection of study data and follow-up of participants through study completion*<br>• *Development and maintenance of all study materials including the MOOP and study forms*<br>• *Maintenance of the study binder (regulatory and study documents)*<br>• *Retaining specific records, (e.g., laboratory or drug distribution records)* |

**Roles Checklist**

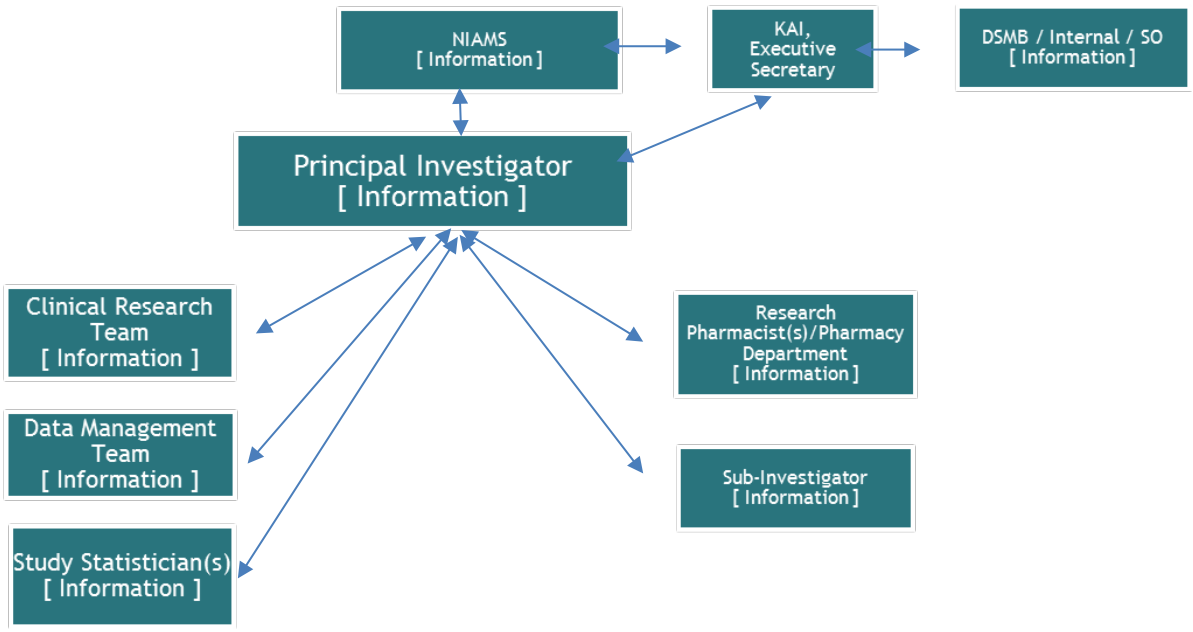
- **Principal Investigator**
- **Study Coordinator**
- **Back-Up Study Coordinator**
- **[insert roles as required by protocol]**

**Responsibilities Checklist:**

- **Records and files maintenance**
- **Serving as Contact to and Delivering Files to IRB/HRPO**
- **Training staff on study procedures**
- **Data collection**
- **Participant Identification**
- **Participant Screening**
- **Participant Enrollment**
- **Participant Retention**
- **Data Entry**
- **[insert responsibilities as required by protocol]**

## 4.1 Organization Chart

This section of the MOOP should include the study organization chart. It is a diagram that shows the structure of the study and the relationships among the staff members.



## 5.0 Recruitment and Retention Plan

### 5.1 Participant Recruitment

This section of the MOOP should describe how the site will identify and enroll eligible individuals into the study. It should describe the target population, recruitment strategies, screening procedures and inclusion/exclusion criteria.

***Sample Text:***
***The PI and/or study coordinator will pre-screen potential participants by reviewing medical records of patients being followed by the PI in the Arthritis and Musculoskeletal Clinic. The PI will present the study information to the potential participants during a regular clinic visit. If the participant is interested and willing to consent immediately, the PI and/or Study Coordinator will review the informed consent process with the participant. If the participant needs additional time to think about the study and participation, they will be given a copy of the informed consent form (ICF) and any other related IRB study approved document(s). The Study Coordinator will follow up with the potential participant at 1-2 weeks to learn if he/she is still interested and would like to participate. If potential participant is still interested, a screening visit will be scheduled to review the ICF to obtain signatures required to enroll in the study.***

**Recruitment Checklist**:

- **Did you explain how potential participants are identified as potentially eligible?**
- **How/where/when are patients approached?**
    - **Be specific: "Approach the participant in their hospital room during nurse blood draws."**
- **Is the participant recruited through marketing materials, such as a poster?**
    - **Are they instructed to call a number? If so, are they to leave a message, set up an appointment, or something else?**

## 5.2 Participant Retention

This section of the MOOP should describe the plan for participant retention, as well as an action plan for corrective action in case there are problems with retention.

***Sample Text:***
***Every effort will be made by the PI and study team to ensure participants complete each study visit and the study overall. We will use the following strategies to help to maximize retention and minimize loss to follow-up:***

- ***Following a proactive plan for retention, including calling participants to see how they are doing, sending birthday and holiday cards, and providing transportation and child care, as needed***
- ***Building participant relations and participant satisfaction, with the study coordinator taking a central role on this effort e.g. the study coordinator calling the participants on routine schedule to check how they are doing, asking the participant to complete surveys during the study to determine if they are satisfied etc.***
- ***Giving participants and their families the opportunity to ask questions and express concerns pertaining to their condition throughout the study***
- ***Enhancing participant's understanding of the study's objectives and the protocol by reminding the participant of the study aim during study visits or having a questions and answer sessions after each visit, if needed.***
- ***Distributing newsletters to participants to provide feedback information on the status of the study***
- ***Assessing each participant's drop-out potential and intervening as needed to keep participants interested in continuing to participate***

***In the event that a participant does not return for study visits, the PI and/or study coordinator will make several contacts using all of the contact information provided by the participant. This will include sending certified letters to the participant's listed address, if required.***

**Participant Retention Checklist:**
**[Insert Study Team Member(s)] will work to ensure participants complete the entire duration of the research study by employing the following strategies:**

- **[insert incentives]**
- **[insert plan to change incentives in a corrective action should retention be poor]**
- **[insert amount(s) provided for transportation/childcare assistance]**
- **[insert planned reminder schedule]**
- **[insert planned mailings/phone call schedule]**
- **[Refer to Section 6.1 for screening procedures that support retention]**
- **[insert additional items from protocol as relevant]**

## 6.0 Screening and Eligibility Criteria

### 6.1 Screening

This section should detail the screening procedures for determining an individual's eligibility for the study. Frequently, there is a *pre-screening* phase when the study team responds to initial telephone calls from interested individuals or physicians. Such an activity should be included in this section of the MOOP.

***Sample Text:***
***The Study Coordinator will utilize the following steps to screen participants for the study:***

***I. Pre-Screening Phase***
- ***a. Potential participant will call the number on a poster in the Emergency Room advertising the study. This number directs the participant to the Study Team's office phone.***
- ***b. Study team staff will take the participant's phone call and explain the study. If participant is interested, and meets eligibility criteria as outlined in Section 6.3, study staff will set up a screening appointment.***
- ***c. If the participant leaves a message, study staff will return their call and explain the study. If participant is interested, and meets eligibility criteria as outlined in Section 6.3, study staff will set up a screening appointment.***

***II. Screening Phase***
- ***a. Study coordinator will meet with potential participant to explain the study***
- ***b. Study coordinator will ensure that participant meets eligibility criteria as outlined in Section 6.3***
- ***c. Study coordinator will probe for participant's ability to complete the duration of the study:***
  - ***i. Is the participant planning to move during the duration of the study?***
  - ***ii. Is the participant looking for a new job?***
  - ***iii. Is the participant in the military, and/or do they have a spouse in the military?***
- ***d. Study coordinator will have the participant sign an Informed Consent Form, HIPAA Authorization Form, and provide copies to participant while placing originals in participant file.***
- *e.* ***Study coordinator will collect contact information, including contact information for one family member and one neighbor.***

## 6.2 Screening Log

A Screening Log documents all individuals evaluated for study eligibility. It generally contains the individual's initials and study identification number (screening number), age, gender, race and ethnicity, screening date, and eligibility status (e.g., eligible for study participation and date enrolled; ineligible for study participation and reason; refused consent and reason). It may also contain the randomization number if different from the screening number.

This section of the MOOP should describe the process for entering data in the screening log and the contents of the screening log. A Screening Log should be included as an appendix. (Note: this information is usually part of the reporting requirements for data and safety monitoring plan.)

**Screening Log Checklist:**

- **Consult Protocol for necessary data fields for screening log, including:**
  - **Screening/Identification ID**
  - **Screening Member of Study Team**
  - **Date Screened**
  - **Identifying Characteristics (Demographics)**
  - **Eligibility Status**
  - **[Insert Additional Study-Centric Information]**

**Sample Screening Log:**

| Screening ID | Screened By | Age | Gender | Race / Ethnicity | Screen Date | Eligibility Status |
|---|---|---|---|---|---|---|
| T0001 | JD | 71 | F | C | 21/DEC/2015 | Eligible; Declined |
| T0002 | JD | 66 | M | C | 28/DEC/2015 | Eligible; Enrolled 28/DEC/2015 |
| T0003 | MO | 70 | F | AA | 04/JAN/2016 | Ineligible; Unable to Make Own Medical Decisions |
| T0004 | JD | 78 | F | C | 09/JAN/2016 | Eligible; Declined due to Moving Away |

**Screening Log Procedure Checklist:**

1. **Is this log kept on paper, electronic format, or both? Detail this procedure.**
2. **Where is an electronic copy of the screening log template?**
3. **What is the procedure for updating/editing the screening log?**
   a. **Who is responsible for reviewing/approving changes?**
   b. **What is the naming convention for the file?**
   c. **Where is the file kept so that the study team may access it and previous versions?**
4. **Data entry:**
   a. **Who is responsible?**
   b. **What system is used for data entry?**
   c. **Where are entered logs stored? How are they denoted?**

## 6.3 Eligibility Criteria

Study eligibility is determined by a set of inclusion and exclusion criteria described in the study protocol. Potential participants must meet all entry criteria prior to enrollment, and not meet any of the exclusion criteria. This section of the MOOP must define the method for determining eligibility (e.g., blood pressure sitting down). It also should list the forms that must be completed to document eligibility (e.g., medical history form, physical examination form).

***Sample Text:***
***Study eligibility is determined by inclusion/exclusion criteria:***

***Inclusion Criteria***

- ***Age 18-90***
- ***Diagnosis of Osteoporosis***
- ***Must pass screening quiz to establish that they can make their own medical decisions***
- ***Must pass routine Physical Examination***

***Exclusion Criteria***

- ***Must live locally, and be able to attend 20 scheduled visits and 3-month phone follow-up***
- ***Must not be under 18, or over age 90***
- ***Must not be pregnant***
- ***Must be able to read and speak English***

***If the participant does not meet all the above criteria, he/she will not be eligible for study participation.***

## 7.0 Informed Consent and HIPAA

This section of the MOOP should describe the specific instructions for obtaining informed consent. If there are multiple consent documents (e.g. collecting data from additional sources, participation in ancillary studies), then each informed consent form should be outlined in the MOOP and accompanied by detailed instructions, which should include the following:

- When and where consent will be obtained
- Role of the person that will discuss the nature of the study with the individual and sign the consent form
- Will the participant be given sufficient time to review the consent form; and a description of what procedure would be followed if the participant needed additional time to review to consent form [e.g., additional time provide at first meeting time on site, take consent document home and return; when returned, how returned [e-mail, fax, in-person]
- When a copy of the signed consent will be given to the individual and where the original signed copy of the consent will be stored
- Re-consent process if participants need to be re-consented at any time during the study.

The IRB-approved Informed Consent Form should be included as an appendix in the MOOP. For more information/guidance on how to create an informed consent, please refer to the OHRP guidance on Informed Consent and OHRP Informed Consent Checklist.

***Sample Text:***

- ***Study Informed Consent Form: General description of the study and participant's responsibilities – page 34, Appendix Item A***
    - ***Administered by Study Coordinator at Scheduled Screening Visit at C.F. Memorial Hospital, Suite 535B***
    - ***Coordinator explains risks and benefits, reminding patient participation is voluntary, and may discontinue at any time (and procedure for termination).***
    - ***Coordinator provides contact information in case of medical emergency due to study participation, or for questions about subject rights.***
    - ***Coordinator explains who has access to patient's protected health information, and how confidentiality is maintained.***
    - ***Coordinator explains any costs participation may incur.***
    - ***Coordinator explains how participant may learn outcome of study, and be provided with a copy of publication of any article published***
    - ***Copies of signed ICF will be provided to participant, and placed in her or his file.***

## 7.1 HIPAA Authorization

The Health Insurance Portability and Accountability Act (HIPAA) is the legislation that sets forth the Privacy Rule that protects participant confidentiality. According to the Privacy Rule, participants must authorize investigators, IRBs, research administrators, and others before their Protected Health Information (PHI) can be used for research purposes.

If the study is collecting any personally identifiable health information, these items should be explained in this section of the MOOP. Additionally, the IRB-approved HIPAA form should be included as an appendix. If it is not IRB-approved when the MOOP is submitted to the NIAMS, it should be submitted at a later date.

The format of the HIPAA authorization is dictated by the local IRB, meaning that it can be a separate document from the ICF, reviewed and signed by the participant in addition to reviewing and signing the ICF. Investigators should review information provided in Impact of the HIPAA Privacy Rule on NIH Processes Involving the Review, Funding, and Progress Monitoring of Grants, Cooperative Agreements, and Research Contracts and Protecting Personal Health Information in Research: Understanding the HIPAA Privacy Rule, NIH Publication 03-5388 at http://privacyruleandresearch.nih.gov/pdf/HIPAA_Booklet_4-14-2003.pdf.

***Sample Text:***
***The study coordinator will be collecting your protected health information (PHI) for use in this study and any future uses you have agreed to as specified in the consent form you have already signed. Please review and sign the attached authorization form to allow the study team to access your PHI. Your information will only be accessed as needed to schedule appointments and collect study-relevant data. This information may include your name, age, home address, and phone number.***

**HIPAA Checklist**:
**This study will collect the following information that could potentially identify the participant. This information will be collected and used only for research purposes, and will only be made accessible to study staff (examples):**

- **Name**
- **Date of Birth/Age**
- **Home Address, including Zip Code**
- **Phone Number(s)**
- **Qualifying Medical Condition for Inclusion into Research Study**

## *8.0* Study Intervention

This section of the MOOP should include a detailed description of the study intervention and how it will be implemented. It must be described clearly so that all participants consistently receive the intervention as specified in the protocol.

A study intervention can be defined as a drug, supplement, biologic, gene transfer, vaccine, device, procedure (e.g., surgery), behavior (e.g., Internet-based education) and/or lifestyle change (e.g., diet, exercise) introduced to prevent or change the natural course of a disease or condition. A clinical trial has an intervention that is assessed for efficacy and/or safety.

**Types of Examples:**

- **For drug, vitamin, or other supplement, biologic, gene transfer, and vaccine intervention studies**, the distribution, preparation and handling, labeling, and administration are detailed along with the duration of treatment and criteria for treatment discontinuation. Information on regulatory approval applicable to the use of unapproved drugs clinical trials is provided in the Code of Federal Regulations Title 21, Part 312 , revised as of April 1, 2017 https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRsearch.cfm?CFRPart=312 This section must include the regulatory approval status of the drug, whether it is a new indication/population or approved for the disease/condition under study. A detailed description of the information that must be provided is documented in the ICH E6 Guideline for Good Clinical Practice. This document is available on the Internet at http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf
- **Device studies** require a detailed description of the device and its intended use. This section must include the regulatory approval status of the device, and whether it has an investigational device exemption. Information on device studies is provided in the Code of Federal Regulations (CFR) Title 21, Part 812, revised as of April 1, 2017, at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=812&showFR=1
- **Procedure studies** (e.g., surgery) require a detailed description of the procedure(s).
- **Behavior** and **life style studies** require a detailed description of the intervention as well as documentation of the process.

***Sample Text:***

***The study intervention for Effects of Instructor-Led Exercises on Improved Osteoporosis Outcomes is an experimental set of exercises. This life style study consists of two exercises taught to the participant by a physician in order to potentially improve osteoporosis outcomes.***

1. ***The participant will have range of motion measured by their physician.***

2. ***The physician will demonstrate and then lead the participant in stretching and the 2 intervention exercises.***
3. ***The participant will be provided a journal to record daily at-home exercises, and record any discomfort.***
4. ***At each subsequent visit, the physician will again demonstrate and lead the participant in stretching and exercises to ensure the participant is performing the intervention correctly at home. The physician will then review the participant journal together with participant at each visit, and discuss any instances of discomfort.***

## 9.0 Randomization

This section of the MOOP should describe the randomization procedures including but not limited to:

- ***Randomization Plan*:** The method used for generating randomization codes to assign participants to treatment groups.
- ***Process Responsibilities*:** The individual who maintains the master randomization list must be identified. This person is responsible for assigning randomization codes, notifying appropriate study staff that the participant has been randomized, and securely storing all randomization files.
- ***Procedure for Randomizing a Participant:*** The individual who is responsible for initiating the randomization procedure must be identified. This individual must know whom to contact once a participant is determined eligible for a study, and which forms must be completed prior to randomization (e.g., informed consent form and participant eligibility form).

Randomization assignments must be documented so that they can be reviewed during a data review or audit. Some studies maintain the assigned and masked randomization code in the study computer system while other studies maintain the assignment in a randomization log. In either case, the method for documenting randomization must be described, and if relevant, a person named who will be responsible for completing the randomization log at the site.

***Sample Text:***
***The Statistician will be responsible for generating randomization codes.***

***Method:***

1. ***The Statistician will be notified of a new eligible participant by the Study Coordinator.***
2. ***The Statistician will use a pre-printed binder of randomized codes, locked in office 308F, cabinet C, using the next available code. The key, marked 308F-C, is stored in the research office, locked in the safe.***
3. ***The Study Assistant will transfer this code to the screening log, and notify the Study Coordinator that the randomized code is available.***

***The Statistician will maintain the master randomization list, assign randomization codes, notify appropriate study staff regarding randomization, and securely store randomization files. The Study Coordinator will initiate randomization procedure, and must know who to contact once a participant is deemed eligible for the study, including which forms to complete prior to randomization.***

**Randomization Checklist:**

- **Was the method of randomization described in step-by-step detail?**
- **Was the responsibility for generation of a randomized code detailed?**
- **Who maintains the master randomization list?**
- **Who assigns randomization codes?**
- **Who notifies study staff regarding randomization?**
- **Who is contacted regarding eligible participants? What is the chain of communication?**
- **What forms must be pre-completed prior to randomization? Prior to enrollment?**

## 9.1 Investigational Product Activities

This section of the MOOP should describe how the investigational agent is to be stored, prepared, dispensed, and returned or destroyed. It should provide instructions for completing drug accountability records and administrative records.

If an investigational product is maintained by someone other than the study team, (i.e. the pharmacy, etc.) the MOOP should provide guidance on tracking product maintenance guidelines as received.

***Sample Text:***
***The University of Medicine Pharmacy Department will maintain the experimental study medication in a locked refrigerator in room 305B. It will be stored at 36 degrees Fahrenheit at all times, to be checked twice a day by pharmacy staff. The study staff will check the refrigerator temperature log on Mondays and Wednesdays to ensure that the logs are being completed. In the event the refrigerator temperature was noted to be above 40 degrees Fahrenheit, the study team will contact the drug provider for guidance immediately.***

***The study medication should be stored in a refrigerator at all times (when not being administered), to be stored between 34 and 36 degrees Fahrenheit. The study medication should not be exposed to light. Unused or discarded study medication should be returned to the drug provider at the following address in a dry ice package:***

***ATTN: Dr. Lawrence Howser***
***Nani-Tech Industries, LLC***
***304545 Trade Avenue***
***Suite 4***
***Chicago, IL  60652***

***Product maintenance guidelines (version date 01APR2015) were received from the University Pharmacy Department on 01 May 2015. These guidelines are reviewed quarterly. As guidelines are revised, new versions are provided to study teams with investigational products on the 1$^{st}$ of the month of the next quarter. Each version received will be stored in the study binder.***

## 10.0 Masking and Unmasking

This section of the MOOP should describe in details the Investigator's procedures for unmasking.

In most studies with randomization, participants and the treating physician are "masked" to the treatment and do not know if the participant is receiving the experimental or a control intervention. In some instances, the study statistician and/or a designated study staff member may securely maintain the randomization codes so the treatment assignments are not known. The masking/unmasking procedures must be determined prior to the enrollment of the first participant.

Unmasking is a serious action and should be limited to reduce potential bias and maintain the integrity of the data. The MOOP should clearly state who is has access to masked and/or unmasked on the study team. Additionally, the handling of the masked data, including preparation of masked reports, should be described in this section.

***Sample Text:***

1. ***Upon enrollment, the Study Coordinator must notify the Pharmacy of the intent to deliver the intervention within the specified time frame of <30 minutes by placing a call to (308) 334-2397.***
2. ***The Pharmacy must acknowledge the notification with an email to the research department, and assurance that the intervention drug will be provided, masked, within 30 minutes to the Study Coordinator's location (patient bedside).***
3. ***Upon delivery, the Study Coordinator will sign for the masked drug.***
4. ***Upon signature, the Pharmacy will notify the research department by email.***
5. ***The intervention drug is provided to the physician to be administered to the patient.***
6. ***Label from the intervention drug is saved and added to the label collection page of the study binder.***

In the event that unmasking occurs, the following should be recorded:

- The identification of the unmasked participant,
- The reason for unmasking,
- The study staff person responsible for unmasking, and
- A list of person(s) who are not masked.

## 11.0 Participant Evaluations and Follow-Up

Once a participant is enrolled in the study, there are typically baseline and follow-up assessments. This section of the MOOP should describe those study procedures. It should also include all assessments as appendix items, as well as their schedule and the procedures for obtaining data. All endpoint or outcome evaluations (e.g., improvement in symptoms) and safety evaluations (e.g., blood chemistries) should be identified. The schedule of when evaluations take place must also be specified (e.g., five hours after the last dose of study drug/placebo administration).

### 11.1 Timeline and visit schedule

A useful study tool included in the MOOP is a schedule of visits and evaluations that specifies what is to be done at each study phase and at each contact with the study participant. An example of a schedule is provided in **Appendix A**. Please add the study visit schedule in this section of the MOOP.

**Sample schedule:**

| **Participants Assigned to Treatment Group** | | |
|---|---|---|
| **Timepoints** | **Location** | **Activities at Timepoint** |
| Timepoint 1: Baseline Data Collection | Clinic | Patient will have initial assessment with physician and receive intervention drug. Data will be collected using SSDII assessment form. Patient will be observed for 1 hour for any side effects. |
| Timepoint 2: 3-Month Follow-Up | Clinic | Patient will receive 2nd dose from physician, and have brief follow-up assessment using SSDII-B form. Patients will be observed for 1 hour for any side effects. |
| Timepoint 3: 6-Month Follow-Up | Phone | Patient receives no intervention, has brief follow-up assessment over the phone using SSDII-E form and Satisfaction survey. |

**Timeline and Visit Schedule Checklist:**

- **Have you covered each visit or participant contact?**
- **Have you specified when each takes place?**
- **Have you described study procedures?**
- **Where will each take place?**

## 11.2 Visit Procedures

In this section of the MOOP, each visit should be explained in enough detail so that a new or substitute team member can perform the activity at the visit. Step-by-step procedures should be documented for all study procedures in this section.

**Sample Text:**
***Upon notification that participant has arrived at the hospital waiting room, the Study Coordinator must notify the physician that the participant is ready. The Study Coordinator should then notify the Pharmacy that the participant for the study is present, and arrange delivery of intervention. Refer to Section 10.0 for blinding/unblinding procedures.***

***The Study Coordinator will lead the participant to room 4140C. The Study Coordinator will observe the Physician administering the intervention, and take observational notes as required.***

***Post-intervention administration, the Study Coordinator will perform the SSDII assessment. After completing this assessment, the Study Coordinator will remind the participant of the next scheduled visit, and re-check the participant's contact information for accuracy.***

***Finally, at the end of the visit, the Study Coordinator will escort the participant to the waiting room.***

## 11.3 Follow-up

This section should detail the strategies a site will use to follow participants. Additionally, it should also include details about processes and procedures to follow if a participant discontinues treatment before study completion.

***Sample Text:***

***Participants will be followed through all study visits through the study completion. We will use the following strategies to follow the participants:***

- ***Monthly phone calls,***
- ***Sending birthday cards,***
- ***Sending postcards.***

***In the event a participant discontinues study treatment before study completion, every effort will be made by the study team to have the participant continue to complete all other study procedures. However, if the participant is not willing to continue study participation, the study team will attempt to collect the final visit data.***

## 12.0 Concomitant Medications

Please list all allowable and/or excluded concomitant medications in this section of the MOOP.

**Sample Text:**

***The following includes all the medications that are prohibited during the course of the study:***

- ***Celontin (Methsuximide)***
- ***Felbatol (Felbamate)***

***The following includes all the medications that are allowed during if the participant has been on stable dose 30 days prior to the screening visit and during the study:***

- ***Gabapentin***
- ***Aspirin***

- The form/log used to collect concomitant medication information and the period of time for which this information will be collected should be described (i.e. in the past six months, in the past year, ever etc.) in this section of the MOOP. The form/log should be included as an appendix.

## 13.0 Safety Reporting

This section of the MOOP must detail the definitions of and procedures for reporting adverse events, serious adverse events and unanticipated problems, as applicable.

**Examples of safety reporting follow. Please follow specific guidance at: https://www.niams.nih.gov/grants-funding/conducting-clinical-research/data-safety-guidelines-policies and go to link for How to Write a NIAMS Data and Safety Monitoring Plan.**

**Example Adverse Event (AE) and Serious Adverse Event (SAE) definitions:**

- ***Adverse Event*** - An adverse event is any unfavorable and unintended diagnosis, sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the study intervention, which may or may not be related to the intervention. AEs include any new events not present during the pre-intervention period or events that were present during the pre-intervention period which increased in severity.
- ***Serious Adverse Event*** – A serious adverse event is any untoward medical occurrence that results in death, is life-threatening, requires or prolongs hospitalization, causes persistent or significant disability/incapacity, results in congenital anomalies/birth defects, or, in the opinion of the investigators, represents other significant hazards or potentially serious harm to research participants or others.

## 13.1 Adverse Event Reporting

In this section of the MOOP, the procedure for collecting and reporting AEs should be detailed, including the role of the Principal Investigator and study Medical Monitor (if applicable). In addition, a sample AE form should be included as an appendix.

Requirements for reporting AEs to the NIAMS and the study's independent data and safety monitoring body (i.e., Data and Safety Monitoring Board (DSMB) or Safety Officer (SO), FDA and IRB) should be described in this section.

**Sample Text:**

***Upon notification of an Adverse Event (AE), the Study Coordinator will notify all appropriate parties as described in the protocol:***

1. ***The Study Coordinator will complete the AE form as it exists in Appendix B.***
2. ***The Study Coordinator will immediately notify the Principal Investigator and Medical Monitor via emergency contact information.***
3. ***The Study Assistant will draft a notification email to the IRB and HRPO. The Study Coordinator will review and submit the draft notification to the Principal Investigator.***
4. ***The PI will advise the Study Team regarding screening, enrollment, and ongoing participation.***
5. ***Upon advisement by the IRB, the Principal Investigator will determine the study's status, and notify the Study Team.***

A sample AE form is shown in **Appendix B**. AEs and/or laboratory abnormalities identified in the protocol as critical to participant safety must be reported to the NIAMS and the safety monitoring body. All AEs experienced by the participant during the time frame specified in the protocol (e.g., from the time study drug administration through the end of the study) are to be reported, as outlined in the protocol.

**Checklist:**

- **How are study staff notified of AEs?**
- **Who is responsible for reporting the AE? How soon?**
- **Who does the responsible person for notifying the PI? Medical Monitor? IRB?**
- **After an AE, who determines the status and activities of the study?**

## 13.2 Unanticipated Problems

Unanticipated Problems are not defined in 45 CFR Part 46, but are defined by the OHRP as any incident, experience or outcome that meets all of the following requirements:

1. Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the IRB-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
2. 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
3. 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.

This section of the MOOP should describe the procedures for reporting unanticipated problems, if applicable.

**Sample Text:**

***Upon notification of an Unanticipated Problem, the Study Coordinator will notify all appropriate parties as described in the protocol:***

1. ***The Study Coordinator will immediately notify the Principal Investigator and Medical Monitor via emergency contact information.***
2. ***The Study Assistant will draft a notification email to the IRB and HRPO. The Study Coordinator will review and submit the draft notification to the Principal Investigator.***
3. ***The PI will advise the Study Team regarding screening, enrollment, and ongoing participation.***
4. ***Upon advisement by the IRB, the Principal Investigator will determine the study's status, and notify the Study Team.***

**Checklist:**

- **How are study staff notified of Unanticipated Problems?**
- **Who is responsible for reporting the Unanticipated Problem(s)?**
- **Who does the responsible person for notifying the PI? Medical Monitor? IRB?**
- **After an Unanticipated Problem, who determines the status and activities of the study?**

## 13.3 Serious Adverse Event Reporting

In this section of the MOOP, a plan for SAE reporting to the NIAMS and its contractor will be established. The role of the investigator and study coordinator and any others involved in SAE reporting should be explained in detail. In addition, site-specific SAE report forms should be included as an appendix of the MOOP.

All serious adverse events (SAEs), unless otherwise specified in the protocol and approved by the IRB and the NIAMS, require expedited reporting by the Principal Investigator to the study's safety monitoring bodies and the NIAMS. SAEs must be reported to the independent safety monitoring body and the NIAMS, through the NIAMS Executive Secretary, within 48 hours of becoming known by the Investigator. The immediate reports should be followed by detailed, written reports as soon as possible. Follow up information may be required. All interventional studies, independent of phase or type, must report SAEs. Studies using FDA regulated drugs, biologics or devices must follow FDA reporting requirements.

[Note: multiple reporting requirements, e.g., to the FDA and IRB(s), which are separate from the reporting requirements for the NIAMS and the independent monitoring body, are the responsibility of the Investigator(s) and should be described in this section.] A sample of the SAE form is shown in **Appendix C**.

**Sample Text:**
***Upon notification of a Serious Adverse Event (SAE), the Study Coordinator will notify all appropriate parties as described in the protocol:***

1. ***The Study Coordinator will complete the SAE form as it exists in Appendix C.***
2. ***The Study Coordinator will immediately notify the Principal Investigator and Medical Monitor via emergency contact information.***
3. ***The Study Assistant will draft a notification email to the IRB and HRPO. The Study Coordinator will review and submit the draft notification to the Principal Investigator.***
4. ***The PI will advise the Study Team regarding screening, enrollment, and ongoing participation.***
5. ***Upon advisement by the IRB, the Principal Investigator will determine the study's status, and notify the Study Team.***

**SAE Checklist:**

- **How are study staff notified of SAEs?**
- **Who is responsible for reporting the SAE? Is the 48-hour window noted?**
- **Who does the responsible person for notifying the PI? Medical Monitor? IRB?**
- **After an SAE, who determines the status and activities of the study?**

## 14.0 Data and Safety Monitoring Activities

The roles and responsibilities of the entities monitoring participant safety and study quality should be described in this section, see **Appendix D**. To ensure proper monitoring, the NIAMS has made available a template and guidelines for writing a Data and Safety Monitoring Plan. The template and guidance document can be found at: https://www.niams.nih.gov/grants-funding/conducting-clinical-research/clinical-trial-policies-guidelines-and-templates/data.

## 15.0 Study Compliance

This section of the MOOP should describe relevant deviations/violations and the reporting process to appropriate parties, including the Principal Investigator, the NIAMS, and the safety monitoring entity. The study should adhere to IRB policies for reporting protocol deviations/violations. In addition, the reporting of deviations/violations should be discussed with the NIAMS and the safety oversight entity prior to study start and be clearly outlined in the safety monitoring plan. Protocol deviations/violations impacting participant safety are subject to expedited reporting to the NIAMS and independent safety monitoring body in (e.g., within 48 hours).All events should be reported at the time of the biannual DSMB meeting or submission of the safety report. This section should also describe the mitigation measures that will be taken by the Investigator should protocol deviations or violations occur to ensure no further issues.

**Protocol deviations/violations include, but are not limited to, the following:**

- Enrollment or randomization of an ineligible participant
- Follow-up visit at a time point different from that specified in the protocol
- Failure to obtain Informed Consent
- Entering a participant into another clinical study
- Failure to keep IRB approval up-to-date
- Wrong treatment administered to participant

The study site should maintain a log of all protocol deviations/violations and should report them as specified in the DSMP to the safety monitoring entity. A sample log is presented in **Appendix E** and should be included as an appendix of the MOOP.

## 16.0 Data Collection and Study Forms

This section of the MOOP should describe the study's data collection and data management procedures. Copies of all forms should be included in an appendix. Study forms, also called case report forms (CRFs), provide the vehicle for consistent data collection. In this section of the MOOP, please provide:

**Sample Text:**

***The following documents are used in this study.***

1. ***Standard Satisfaction Discussion Inventory and Inquiry (SSDII)***
    a. ***Developed in 2006 to gauge satisfaction with treatment in patients with spinal issues (Dennis, 2006). 12 Items, Likert Scale. Delivered at each visit.***
    b. ***See: Appendix Item 27***
    c. ***Saved in G:Forms/Assessments/SSDII.pdf***
    d. ***Previous Versions in G:Forms/Assessments/SSDII Past/***
        i. ***Naming Convention: SSDII_DDMMMYYYY_StaffName.doc/pdf***
        ii. ***Responsible for Editing: Any Study Member***
        iii. ***Responsible for Updating/Approving: Study Coordinator***
    e. ***Forms reviewed at monthly team meeting, study team member assigned by department head to edit as needed and submit to study coordinator.***
    f. ***Study Coordinator responsible for study binder creation.***

**Checklist:**

- **Description of each study form and questionnaire**
    - **Copy of each form in the Appendix**
- **How forms are produced and distributed**
    - **Include location on computer/network**
    - **Include naming convention**
    - **Include responsible staff for updating/editing/approving**
- **Maintenance of Forms**
- **Participant binder setup**
    - **Include responsible staff**

## 16.1 Source Documentation

A source document is any document on which study data are initially recorded. Source documents include laboratory reports, Electrocardiography (ECG) tracings, medical records, standardized test forms, etc. These data are then transcribed to a paper CRF or electronic CRF (eCRF) to document study-specific data requirements.

This section of the MOOP should describe how study data are initially collected and maintained for the study. All essential study documents must be retained by the investigator as described in Section 16.3.

***Sample Text:***

1. ***Physical Examination form, signed by participant's physician***
    - ***Received within 30 days after enrollment from participant before receiving intervention, signed and dated. Principal Investigator may contact participant's physician with any concerns.***
    - ***Physician administering intervention uses data from examination form for baseline data; specifically, blood pressure range and complaints of osteoporosis-related pain/discomfort.***
    - ***Filed in participant's study file.***
    - ***At conclusion of study, examination form is kept with study records as required by protocol/IRB guidelines.***

**Sample Checklist:**

- **Source documents (e.g., lab reports, ECG tracings, x-rays, radiology reports, etc.)**
- **Signed consent forms**
- **CRFs**
- **Data correction forms**
- **Workbooks**
- **Questionnaires completed by the participant**

## 16.2 General Instructions for Completing Forms

In this section of the MOOP, if CRFs are used in the study, please provide a set of instructions for completing CRFs to ensure quality and consistency in data collection. Some useful and frequently used examples are listed below:

***Sample Text instructions:***
***Print using black ink when completing study forms. Note, participants must not be identified by name on any study document submitted with the forms (e.g., ECG tracing, lab reports). Replace the participant name with the participant initials and/or identification (ID) number.***

- ***Header: Complete the header information on EVERY page, including pages for which no study data are recorded.***
- ***Participant ID: The participant ID must be recorded on EVERY page, including pages for which no study data are recorded.***
- ***Time: Use a 24 hour clock (e.g., 14:00 to indicate 2:00 p.m.) unless otherwise specified.***
- ***Dates: All dates must be verifiable by source documents. Historical dates are sometimes not known (e.g., date of first symptom); therefore, conventions for missing days and/or months should be described (e.g., UNK or 99).***
- ***Abbreviations: Use of abbreviations not specifically noted in the instructions for completing the forms can be problematic and should be held to a minimum.***
- ***Extraneous Writing: Comments written extraneously on forms cannot be captured in the database; thus, write only in the spaces indicated.***
- ***Correcting errors: If an error has been made on the study forms, place a <u>single</u> line through the erroneous entry and record the date and your initials. Indicate the correct response.***
- ***Skipping items: Do not skip any items. Some items may carry "Unknown" or "Not Applicable" response choices which should be checked when necessary.***
- ***Incomplete data: Data may not be available to complete the form for various reasons. Circle the item for which data is not available and indicate the reason near the appropriate field:***
    - ***If an evaluation was <u>not done</u>, write <u>ND</u> and provide a reason.***
    - ***If the information is <u>not available</u>, but the evaluation was done, write <u>NAV</u>.***

  ***Note: Only in rare circumstances, as in the case of lost documentation, should NAV be recorded on the form. Every effort should be made to obtain the information requested.***
    - ***If an evaluation is <u>not applicable</u>, write <u>NA</u>.***
- ***Incomplete or Illegible forms: Incomplete forms that do not have adequate explanation (as described above) compromise the integrity of the entire study.***

### 16.3 Retention of Study Documentation

The length of time all study files are to be maintained should be specified in this section. In general, federal regulation requires that studies supported by a federal government grant retain participant forms for three years, while studies conducted under a federal contract must retain participant forms for seven years. Please pay special attention to studies involving children, as study documentation retention procedures are often longer in duration and more comprehensive. Details about the federal policies surrounding record retention and access can be found at 2 CFR Part 215. The FDA, IRBs, institutions, sponsors, states, and countries may have different requirements for record retention; investigators should adhere to the most rigorous requirements and should retain forms and all other study documents for the longest applicable period. This specific period should be stated in the MOOP.

**Sample Text:**
***After the study ends, study staff shall maintain participant forms in a secure location for 3 years, as indicated by the protocol, federal regulations, and IRB guidance.***

**Checklist:**
**Regarding this study, how many years must you retain participant forms according to:**

- **The IRB of record?**
- **The FDA?**
- **The sponsor?**
- **The state in which the study was conducted?**
- **The country in which the study was conducted?**
- **The institution in which the study was conducted?**

**The answer? The longest period of time stated by one of the above. Double-check if your study involved minors.**

### 16.4 Administrative Forms

In this section of the MOOP, please list (in bullet format) the study forms that will be used. Include all administrative forms (e.g. Telephone Contact Log, Screening Log, Participant Identification Code List, and Site Visit Log) that assist with study documentation and operations.

## 17.0 Data Management

This section of the MOOP should describe the data management approach and computer system, if applicable, that will support the study. It should detail how data are to be entered (if eCRFs are used), edited, and/or corrected.

Investigators are encouraged to utilize computer systems that encompass the following functions:

- ***Data Tracking*** - to provide the status of enrollment, number of forms completed.
- ***Data Entry -*** that is easy to use and minimizes errors, such as facsimiles of the forms.
- ***Data Editing*** - that identifies out-of-range and missing entries, errors in dates and logical inconsistencies (e.g., first treatment date precedes protocol start date or protocol specifies an examination before randomization, but the examination form is missing).
- ***Updating*** - to correct data and maintain an audit trail of all data changes.
- ***Reporting -*** to describe/account for accrual, forms entered and completed, etc.
- ***Statistical Analysis*** – mechanism to transmit data to statistical analysis packages (e.g., SAS).

This section should also provide detail description of the data flow, handling of error identification and resolution, identification of useful reports, and deriving a frozen, analytic database from edited or "clean" records.

**Sample Text:**
***The BON system, or Binary Online Network, is a data entry system that captures simple patient vital signs utilizing a keyboard number pad only. Any staff can enter this using the BON iPhone App while standing next to a patient bed. Data correction and edits can be done by emailing an app-taken photo of vital signs to the systems administrator. Data dumps of vital signs for individual patients can be sent to departmental email through the app.***

Investigators should be aware that systems of studies that will be submitted to the FDA must be documented and validated Guidance for electronic systems is found on the FDA website, Title 21 Code of Federal Regulations (21 CFR Part 11) Electronic Records; Electronic Signatures-Scope and Application.

## 17.1 External Data

External data refers to data sent to or collected at a laboratory or imaging facility (e.g., blood samples, MRIs, etc.). This section of the MOOP should describe how this information will be collected, labeled, handled, shipped, tracked and reconciled, so that study data are not lost. As stated in the Health Insurance Portability and Accountability Act (HIPAA) guidelines, personal identifiers such as name, geographic location, social security number, and fifteen other specific individual identifiers should not be used (see page 22 above). Therefore, it is important to specify how participant materials will be identified (e.g., by participant identification number) during transmission.

***Sample Text:***

- ***X-Ray of Spine***
    - ***Collected by Radiology at Hospital Center on Patient's Initial Visit***
        - ***2 Standard Images are transferred via departmental envelope to physician by Hospital Administrative staff***
        - ***Images are de-identified by Radiology***
        - ***Images are labeled with Study ID by Study Coordinator at arrival to physician's office***
        - ***Images are kept in a separate locked cabinet in research office***

**External Data Checklist:**

- **How did you ensure all patient identifiers were removed?**
- **Where are samples located? Are they secure?**
- **How are samples transferred?**

## 17.2 Quality Control Procedures

This section should detail the various aspects of the quality control (QC) plan for the study and describe any training and certification procedures. It may include standard operating procedures (SOPs), data and forms checks, monitoring, routine reports, and correction procedures.

### 17.2.1 Standard Operating Procedures (SOPs)

SOPs which relate to conduct of clinical trials should be listed in this section of the MOOP. Note: printed SOPs should not be inserted in the MOOP; printed versions of SOPs should be limited to maintain version control. The location of each SOP (i.e., electronic file name) can be included in this section.

The SOPs should be kept in a central location and made easily available to staff.

### 17.2.2 Data and Form Checks

This section of the MOOP can provide a summary of data and form checks that will be implemented for data quality control. Data quality control checks may identify potential data anomalies such as:

- Missing data or forms
- Out-of-range or erroneous data
- Consistent and logical dates over time
- Data consistency across forms and visits
- Completion of all fields of a "completed form" or reason noted for no data
- Completion of all required forms or reason noted for no data

### 17.2.3 Site Monitoring

The following section should describe site monitoring which is separate from the data and safety monitoring activities described in *Section 14.0 Data and Safety Monitoring Activities*.

Site monitoring may take place through periodic site visits conducted during the study. The frequency of visits may depend upon the site's performance and the number of participants enrolled.

In this section of the MOOP, describe each site’s plan for monitoring, including a monitoring timeline.

## 18.0 Reports

The NIAMS will specify the type and frequency of reports (monthly, administrative etc.) it wishes to receive. Other reporting requirements to local IRBs and study officials should also be described in this section. Reports are also provided to the DSMB, OSMB, or Safety Officer, as applicable, who can specify the format and content of the reports they wish to receive.

In this section of the MOOP, please discuss the types and frequency of the reports that will be prepared, and the members of the study team who will be responsible for completing them.

***Sample Text:***

- ***Enrollment Report***
  - ***Delivered to DSMB within 7 days after 1st enrollment***
  - ***Produced by Study Assistant***

## 19.0 Study Completion and Closeout Procedures

Study close-out activities are performed to confirm that the site investigator's study obligations have been met and post-study obligations are understood. This section of the MOOP should briefly outline the Study Completion and Close-out procedures. Details should be included in the subsequent sections.

***Examples of Close-out activities include, but are not limited to, the following:***

- ***Verification that study procedures have been completed, data have been collected, and study intervention(s) and supplies are returned to the responsible party or prepared for destruction***
- ***Assurance that all data queries have been completed***
- ***Assurance that correspondence and study files are accessible for external audits***
- ***Reminder to investigators of their ongoing responsibility to maintain study records and to report any relevant study information to the NIAMS***
- ***Assurance that the investigator will notify the IRB of the study's completion and store a copy of the notification***
- ***Preparation of a report summarizing the study's conduct***
- ***Participant notification of the study completion***

Additional close-out activities can be found in **Appendix F**.

### 19.1 Participant Notification

In this section of the MOOP, please include the site's plan to notify participants when the study is complete. The Principal Investigator and study staff should develop a plan to notify participants that the study is over, ask whether they would like to be informed of the results, and thank them for their participation. It may include either the first article or a reference to the article.

If there is a written script to be used in a form of a letter/email to participants, that should be included in this section.

## 20.0 Policies

This section of the MOOP should contain all policies relevant to the management of the study, for example policies regarding confidentiality and publication.

### 20.1 Confidentiality Procedures

This section of the MOOP will discuss the safeguards that have been put in place by the PI to ensure participant confidentiality and data security. It is the responsibility of the Principal Investigator to outline and enforce participant confidentiality and data security guidelines. The following is a list of study participant confidentiality safeguards:

- ***Electronic files –*** data identifying participants that are stored electronically should be maintained in an encrypted form or in a separate file.
- ***Forms -*** forms or pages containing personal identifying information should be separated from other pages of the data forms.
- ***Data listings -*** participant name, name code, hospital chart, record number, Social Security Number, or other unique identifiers should not be included in any published data listing.
- ***Data distribution*** - data listings that contain participant name, name code, or other identifiers easily associated with a specific participant should not be distributed.
- ***Data disposal*** - computer listings that contain participant-identifying information should be disposed of in an appropriate manner.
- ***Access*** - participant records should not be accessible to persons outside the site without the express written consent of the participant.
- ***Storage -*** study forms and related documents retained both during and after study completion should be stored in a secure location. If computers are used to store and/or analyze clinical data, the investigator should address the following elements of computer security to ensure that the data remain confidential:
- ***Passwords*** - Passwords provide limitations on general access to computer systems and to the functions that individuals can use. Passwords should be changed on a regular basis.
- ***User Training -*** Study staff with access to clinical computer systems should be trained in their use and in related security measures. Training should include explanations of how to access the system and a discussion of the need for, and importance of, system security.
- ***System Testing -*** Prior to the use of a new computer system, and after any modifications, the system should be tested to verify that it performs as expected. Testing should verify that the password-activated access system performs as intended.
- ***System Backups*** - Backup copies of electronic data should be made at specified intervals. Backups should be stored in file cabinets or secure areas with limited access. Storage areas should have controlled temperature (i.e. approximately 68°F (20°C)) and relative humidity (i.e. 50%) so that backup tapes are not damaged.

### 20.2 Publications

Investigators have a responsibility to the public to make study results available as soon as possible. This section of the MOOP should detail the study's publication policy so data are not released inappropriately, authorship is predetermined, and manuscripts are subjected to rigorous review before they are submitted for publication.

Any plans to publish study results prior to study completion should be reviewed by the NIAMS and the study's DSMB to ensure study integrity is maintained.

## 21.0 MOOP Maintenance

This section should describe the procedures for updating and distributing updated MOOP versions, as well as staff members responsible for this activity.

> The footer on each page of the MOOP should include the PI's last name, type of MOOP, version number, date and page number e.g. "*Brown_Single Site MOOP_v 1.0 24Mar2017….Page 2 of 30*" to facilitate any changes and/or additions.

The MOOP may serve as a history of the project, documenting the time and nature of any changes in procedures and policies. Electronic version control must also be maintained along with an archive of previous versions.

The MOOP should be continuously reviewed by study staff to ensure the operating procedures described are accurate. If any procedures have been changed or modified, the MOOP should be updated and the revised document distributed, with instructions, for replacement in the MOOP. See **Appendix G** for a sample versioning page. This should be the first page of the MOOP.

## SUMMARY

The development of a study MOOP is an important process that yields a product that is critical in ensuring a study with high quality results. The MOOP leads study staff to learn the details of the study and to develop precise procedures that are understood and followed during the study.