National Institute on Aging (NIA)

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

*Version 2.0 – December 2020*

Table of Contents

[ACRONYM GLOSSARY 4](#_Toc58953527)

[INTRODUCTION 7](#_Toc58953528)

[HOW TO USE THIS DOCUMENT 8](#_Toc58953529)

[Overview 9](#_Toc58953530)

[MOP Contents and Organization 11](#_Toc58953531)

[1.0 Introduction 11](#_Toc58953532)

[2.0 Study Overview 12](#_Toc58953533)

[3.0 Study Organization and Responsibilities 13](#_Toc58953534)

[*Table 1: Sample Staff Roster* 14](#_Toc58953535)

[4.0 Study Flow 16](#_Toc58953536)

[Figure 1: Study Flow Diagram 16](#_Toc58953537)

[5.0 Informed Consent 17](#_Toc58953538)

[5.1HIPAA Authorization 18](#_Toc58953539)

[6.0 Recruitment and Retention 19](#_Toc58953540)

[6.1 Participant Recruitment 19](#_Toc58953541)

[6.2 Participant Retention 19](#_Toc58953542)

[7.0 Screening and Eligibility Criteria 21](#_Toc58953543)

[7.1 Screening 21](#_Toc58953544)

[7.2 Screening Log 22](#_Toc58953545)

[7.3 Eligibility Criteria 23](#_Toc58953546)

[8.0 Study Intervention 24](#_Toc58953547)

[9.0 Randomization 26](#_Toc58953548)

[9.1 Investigational Product Activities 27](#_Toc58953549)

[10.0 Blinding and Unblinding (Masking and Unmasking) 28](#_Toc58953550)

[11.0 Study Measurements and Procedures 29](#_Toc58953551)

[**11.1 Timeline and visit schedul*e*** 29](#_Toc58953552)

[**11.2 Visit Procedures** 30](#_Toc58953553)

[**11.3 Follow-up** 30](#_Toc58953554)

[**11.4 Final Study/Early Discontinuation Evaluations** 31](#_Toc58953555)

[12.0 Concomitant Medications 32](#_Toc58953556)

[13.0 Safety Reporting 33](#_Toc58953557)

[**13.1 Adverse Event Reporting** 33](#_Toc58953558)

[**13.2 Unanticipated Problems** 34](#_Toc58953559)

[**13.3 Serious Adverse Event Reporting** 35](#_Toc58953560)

[14.0 Study Compliance 37](#_Toc58953561)

[15.0 Data Collection and Study Forms 38](#_Toc58953562)

[15.1 Source Documentation 38](#_Toc58953563)

[15.2 Study Forms 39](#_Toc58953564)

[15.3 General Instructions for Completing Forms 39](#_Toc58953565)

[15.4 Data Flow 40](#_Toc58953566)

[15.5 Administrative Forms 40](#_Toc58953567)

[15.6 Retention of Study Documentation 41](#_Toc58953568)

[16.0 Data Management 42](#_Toc58953569)

[16.1 External Data 42](#_Toc58953570)

[16.2 Quality Control Procedures 43](#_Toc58953571)

[16.2.1 Standard Operating Procedures 43](#_Toc58953572)

[16.2.2 Data and Form Checks 43](#_Toc58953573)

[16.2.3 Site Monitoring 44](#_Toc58953574)

[17.0 Data and Safety Monitoring Activities 45](#_Toc58953575)

[17.1 Reports 45](#_Toc58953576)

[17.2 Study Completion and Close-Out Procedures 45](#_Toc58953577)

[17.2.1 Participant Notification 46](#_Toc58953578)

[17.2.2 Confidentiality Procedures 46](#_Toc58953579)

[17.2.3 Publications 47](#_Toc58953580)

[18.0 MOP Maintenance 48](#_Toc58953581)

[*SUMMARY* 48](#_Toc58953582)

[Appendix A - Sample Schedule of Events 49](#_Toc58953583)

[Appendix B - Sample Protocol Deviation/Violation Log 50](#_Toc58953584)

[Appendix C - Examples of Administrative Forms 51](#_Toc58953585)

[Appendix D - Sample MOP Modification Log 52](#_Toc58953586)

[Appendix E - NIA Single-Site Clinical Trial Sample Closeout Procedures 53](#_Toc58953587)

# ACRONYM GLOSSARY

***Adverse Event (AE) –*** Any untoward or unfavorable medical occurrence in a clinical research study participant, including any abnormal sign (e.g. abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participants’ involvement in the research, whether or not considered related to participation in the research.

***Case Report Form (CRF) –*** A printed, optical, or electronic (eCRF) document designed to capture all protocol-required information for a study.

***Code of Federal Regulations (CFR)******–*** Is an annual codification of the general and permanent rules published in the Federal Register by the executive departments and agencies of the Federal Government.

***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.

***Data and Safety Monitoring Board (DSMB) –*** A group of individuals independent of the study investigators that is appointed by the NIA to monitor participant safety, data quality and to assess clinical trial progress.

***DHHS* –** Department of Health and Human Services

***Electrocardiogram (ECG)*** ***–*** A record or display of a person's heartbeat produced by electrocardiography.

***Food and Drug Administration (FDA) –*** An agency within the U.S. Department of Health and Human Services (DHHS) responsible for protecting the 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) –*** A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported 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 –*** The first comprehensive Federal protection for the privacy of personal health information. The Privacy Rule regulates the way certain health care groups, organizations, or businesses, called covered entities under the Rule, handle the individually identifiable health information known as protected health information (PHI).

***ID* –** Identification

***Informed Consent Form (ICF) –*** A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject’s decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form.

***Institutional Review Board (IRB)/Independent Ethics Committee (IEC) –*** An independent body constituted of medical, scientific, and nonscientific 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 material to be used to obtaining and documenting informed consent of the trial participant.

***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 Procedures (MOP) –*** A “cook book” that translates the protocol into a set of operational procedures to guide study conduct. A MOP is developed to facilitate consistency in protocol implementation and data collection across study participants and clinical sites.

***NIA –*** National Institute of Aging

***NIH******–*** National Institutes of Health

***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

***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.

***Package Insert* –** A compilation of the clinical and nonclinical data on the investigational product(s) that is relevant to the study of the investigational product(s) in human subjects.

***Principal Investigator (PI) –*** The individual with primary responsibility for achieving the technical success of the project, while also complying with the financial and administrative policies and regulations associated with the 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 sponsored research award rests with the Principal Investigator.

***Protected Health Information (PHI)*** ***–*** A subset of individually identifiable health information, oral or recorded, relating to a subject’s past, present, or future physical or mental health or condition (e.g., medical or research record). The institutional review board (IRB) or Privacy Board may determine what is considered PHI; however, in general, PHI includes health information that is linked to identifiers of the individual or of relatives, employers, or household members of the individual. Some common identifiers of health information include names, social security numbers, addresses, and birth dates, among others.

***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* *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 NIA Program Director regarding participant safety, scientific integrity and ethical conduct of a study.

***Serious Adverse Event (SAE) –*** Any adverse event that:

* Results in death
* Is life threatening, or places the participant at immediate risk of death from the event as it occurred
* Requires or prolongs hospitalization
* Causes persistent or significant disability or incapacity
* Results in congenital anomalies or birth defects
* Is another condition which investigators judge to represent significant hazards

***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 purpose of this document is to provide a Manual of Operating Procedures (MOP) template for Principal Investigators of single-site clinical trials. NIA defines a single-site study as a trial that is conducted by a single funded institution implementing a trial. The role of the MOP is to facilitate consistency in study implementation and data collection across study visits and participants. Use of the MOP 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.

In preparing the MOP, the Principal Investigator must be aware of the terms of award with respect to required reporting, data and safety monitoring, and Institutional Review Board (IRB) approval (see [*NIA Guidance on Clinical Trials*](http://www.nia.nih.gov/research/dea/implementation-policies-human-intervention-studies)*).* All staff members participating in the conduct of this study at participating institutions should have ready access to the MOP and be trained on contents.

The protocol, case report forms (CRFs), informed consent documents, and administrative forms (e.g., screening and enrollment log, protocol deviation log, etc.) should be finalized before the development of the MOP. Additionally, the MOP should be drafted prior to study commencement.

# HOW TO USE THIS DOCUMENT

This is a template and guidance document to be used by investigators developing a MOP for clinical studies supported by the National Institute of Aging and (NIA). Please read this document to understand how to create your study specific MOP. Note that the contents provided in **this document are informational, and include examples of how to develop your study-specific MOP**. If a particular section is not relevant to your particular study, there is no need to include it. Refer to the MOP Outline and Guide on page 12 for the elements that are expected to be included in your study specific MOP.

The sample texts are provided as examples to help you develop your MOP content. Upon completion of each section of your MOP, 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 MOP serves as a reference and handbook that details a study’s conduct and operations. Its purpose is to provide the operational detail to ensure that study procedures are carried out consistently. The MOP is intended to serve as a study “cookbook” that facilitates adherence to study procedures to promote high quality research and to help clinical investigators comply with federal regulations and procedures, and good clinical practice (GCP).

The study team (investigators, coordinators, statisticians, etc.) develops the MOP before the study can commence and keeps it updated throughout the study to record and implement amendments to the protocol and to document refinement of procedures.

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

During a study's planning phase, the Principal Investigator and study staff draft the protocol. The protocol must be approved by the Institutional Review Board (IRB) of record for the study, and by the Data and Safety Monitoring Board (DSMB) or Safety Officer (SO). Prior to developing the MOP, the final protocol, CRFs, informed consent forms, and administrative forms (e.g., screening and enrollment log, protocol deviation log, etc.) should be finalized. Additionally, if the study is to be submitted to the Food and Drug Administration (FDA) under an Investigational New Drug Application (IND), an Investigator's Brochure (for investigational products) or Package Insert (for marketed drugs) must be included. The timeline for the development of study materials must be planned for and typically takes approximately six months.

Development of the MOP requires the involvement of the Principal Investigator and study staff to ensure that the MOP accurately describes how the study procedures will be performed. In multi-site clinical studies, a Steering Committee comprised of the study site and coordinating center investigators often finalizes the protocol and develops or oversees the development of the MOP.

The MOP is a dynamic document that will be updated throughout the conduct of a study to reflect any protocol or consent amendments as well as the refinement of the CRFs and study procedures. The MOP should be maintained in a format that allows it to be easily updated and is typically filed in a three-hole binder or kept electronically as a PDF with bookmarks for navigation between sections. For ease of organization, it is recommended that the MOP be subdivided into various sections separated by dividers or sheets of color paper between each section. Each page of a paper copy of the MOP should have the version number and date; electronic versions of the MOP should have consistent naming nomenclature that includes version dates. As pages are revised, an updated version number and associated date will replace the original page(s) in the MOP. All previous versions of the paper and/or electronic versions must be archived. Once approval to begin the study is received, any changes to the MOP, including the new version number and date, should be submitted to the NIA with track changes for easy reference for review and approval before implementation of any modifications.

The MOP 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. A single-site MOP Outline is available on the NIA Toolbox.

# MOP Contents and Organization

**1.0 Introduction**

The MOP details the study procedures and describes the study-specific documents and must be adapted to each study’s specific needs. The MOP should include all the elements listed below, if relevant. A copy of the study protocol should be included as an appendix.

1.0 Introduction

2.0 Study Overview

3.0 Study Organization and Responsibilities

4.0 Study Flow

5.0 Informed Consent

6.0 Recruitment and Retention

7.0 Screening and Eligibility Criteria

8.0 Study Intervention

9.0 Randomization

10.0 Blinding and Unblinding (Masking and Unmasking)

11.0 Study Measurements and Procedures

12.0 Concomitant Medications

13.0 Safety Reporting

14.0 Study Compliance

15.0 Data Collection and Study Forms

16.0 Data Management

17.0 Data and Safety Monitoring Activities

18.0 MOP Maintenance

The MOP should include all of the relevant sections from this list that apply to the specific study. If a section does not apply (e.g., randomization for a study with no randomization), it is not included in the MOP. Additionally, if the study involves a drug intervention, either the Package Insert for an approved drug or the Investigator’s Brochure for an investigational product must be included as an appendix.

The following documents should also be included in the MOP appendices: Study Protocol, Study Forms, Informed Consent, and HIPAA, Standard Operating Procedures, Recruitment Flyers, Letters to Participants, etc.

# 2.0 Study Overview

The study protocol, presented as an appendix, provides a scientific rationale of the proposed investigation. In this section of the MOP a brief overview (approximately 500-750 words) of the study protocol should be included.

***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

See the NIA [Protocol](https://www.nia.nih.gov/research/clinical-research-study-investigators-toolbox#startup) Template for protocol for protocol development information.

# 3.0 Study 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.

In a single-site study, the site staff is likely to perform the duties of both the study site and a data coordinating center and the responsibilities include the following as relevant:

* Development and maintenance of all study materials including the protocol, MOP and study forms
* Reporting and monitoring of Adverse Events (AEs) and Serious Adverse Events (SAEs)
* Obtaining informed consent from each participant
* Recruitment, screening, and enrollment of participants
* Development of the randomization scheme and procedures
* Collecting study data and following participants through study completion
* Compliance with and accountability of study intervention Protecting participants' rights
* Submitting documents to regulatory bodies (i.e., IRB or FDA)
* Maintenance of study binder
* Developing and implementing:
* Data management procedures including the data flow and procedures for data entry, error identification and correction
* Quality control procedures
* Reports - enrollment, participant status (e.g., withdrawals), adverse events, independent safety monitoring body reports

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

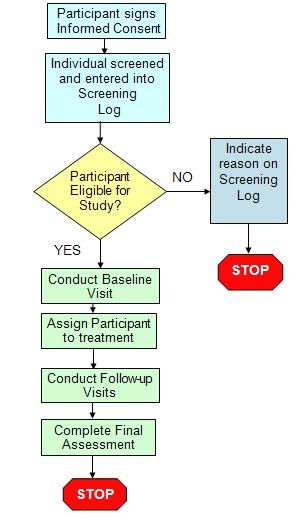
**Responsibilities Checklist:**

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

# 4.0 Study Flow

An overview of the study processes, presented in a flow diagram in Figure 1, describes each of the study's major steps. It should be uniquely tailored to the study and is helpful in describing the study to new staff members.

## Figure 1: Study Flow Diagram



# 5.0 Informed Consent

This section of the MOP describes 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 MOP and accompanied by detailed instructions, which should include the following:

* When and where consent will be obtained
* Role(s) of the person who will discuss the nature of the study with the individual and sign the consent form (i.e. Study Coordinator, PI)
* 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 provided 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 is to be stored
* Re-consent process, if individuals need to be re-consented at any part of the study.

The IRB approved Informed Consent form should be included as an appendix in the MOP.

For more information/guidance on how to create an informed consent, please refer to the [OHRP guidance on Informed Consent](https://www.hhs.gov/ohrp/regulations-and-policy/guidance/informed-consent/index.html" \o "OHRP guidance on Informed Consent, Revised Common Rule), [Revised Common Rule](https://www.hhs.gov/ohrp/regulations-and-policy/regulations/finalized-revisions-common-rule/index.html) and [Impact of Certain Provisions of the Revised Common Rule on FDA-Regulated Clinical Investigations](https://www.fda.gov/media/117042/download). The NIA Informed Consent Template and NIA Informed Consent Checklist, found in the [Study Startup](https://www.nia.nih.gov/research/clinical-research-study-investigators-toolbox?utm_source=staticct&utm_medium=staticct&utm_campaign=staticct#startup) section of the NIA Clinical Research Study Investigator’s Toolbox, provide additional details.

***Sample Text:***

* ***Study Informed Consent Form: General description of the study and participant’s responsibilities –*** 
  + Administered by Study Coordinator at Scheduled Screening Visit at C.F. Memorial Hospital, Suite 535B
  + Study 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 their file.

## 5.1HIPAA 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. The format of the HIPAA authorization is dictated by the IRB of Record, meaning that it may be a separate document from the informed consent, and must be reviewed and signed by the study participant in addition to reviewing and signing the consent form. . A sample form is provided in the Informed Consent Form Template located in the NIA Investigator’s Toolbox. Investigators should review information provided in the “[Impact of the HIPAA Privacy Rule on NIH Processes Involving the Review, Funding, and Progress Monitoring of Grants, Cooperative Agreements, and Research Contracts](http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html)” and contact their appropriate institutional officials to learn how the Privacy Rule applies to them, their organization, and their specific research project. Another helpful resource is “[Protecting Personal Health Information in Research: Understanding the HIPAA Privacy Rule, NIH Publication 03-5388](http://privacyruleandresearch.nih.gov/)”

If the study is collecting any personal identifiable health information, these items should be explained in this section of the MOP. Additionally, the IRB-approved HIPAA form should be included in the appendix.

***Sample Text:***

***The study coordinator will explain to the participant that study coordinator will collect participant’s protected health information (PHI) for use in this study and any future uses the participant has agreed to, as specified in the consent form they have signed. The study coordinator will ask the participant to please review and sign the HIPAA authorization form to allow the study team to access their PHI. Participant information will only be accessed as needed to schedule appointments and collect study-relevant data. This information may include the participant’s 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**

# 6.0 Recruitment and Retention

## 6.1 Participant Recruitment

This section of the MOP should describe how the site will identify and enroll eligible individuals in the study. It should describe the target population, recruitment and retention strategies, screening procedures, and inclusion/exclusion criteria. The NIA Toolbox document [Recruitment and Retention Tips](http://www.nia.nih.gov/sites/default/files/RecruitmentandRetentionTipsFINAL.doc) describes these strategies in detail.

**Sample Text:**

**The PI and/or study coordinator will pre-screen potential participants by reviewing medical records of patients being followed by the PI. 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 a 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?

## 6.2 Participant Retention

This section of the MOP should describe the plan for participant retention, as well as an action plan for corrective action in case there are problems with retention. Plans and suggestions for participant retention should be described and may include strategies such as phone calls, birthday cards, and reminder postcards.

An action plan for correcting retention problems should also be provided in this section.

**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 childcare, 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 question and answer sessions after each visit, if needed.**
* **Distributing newsletters to participants to provide feedback information on the status of the study and intervening as needed to keep participants interested in continuing to participate**
* **Assessing each participant’s drop-out potential**

**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 return receipt letters to the participant’s listed address.**

# 7.0 Screening and Eligibility Criteria

## 7.1 Screening

This section details the screening procedures outlined in the protocol to participant eligibility. If individuals must be enrolled in the study within a specific window of time following completion of the screening procedures, then such requirements should be included in the MOP.

Frequently, there is a *pre-screening* phase during which the study coordinator responds to initial telephone calls from interested individuals or physicians. With consideration for HIPAA regulations, as interpreted by the site’s institution, the PI/study coordinator may access their clinic’s medical records, hospital admission or discharge notes, if necessary, to identify potential candidates for screening.

***Sample Text:***

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

1. Pre-Screening Phase
   1. 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.
   2. 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 7.3, study staff will set up a screening appointment.
   3. 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 7.3, study staff will set up a screening appointment.
2. Screening Phase
   1. Study coordinator will meet with potential participant to explain the study
   2. Study coordinator will begin the process of ensuring that participant meets eligibility criteria as outlined in Section 7.3
   3. Study coordinator will probe for participant’s ability to complete the duration of the study:
      1. Is the participant planning to move during the duration of the study?
      2. Is the participant looking for a new job?
      3. Is the participant in the military, and/or do they have a spouse in the military?
   4. 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.
   5. Study coordinator will collect contact information, including contact information for one family member and one neighbor.

**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 7.1 for screening procedures that support retention]**
* **[insert additional items from protocol as relevant]**

## 7.2 Screening Log

A Screening Log documents all individuals evaluated for study eligibility. It generally contains the individual’s initials, identification number (screening number), age, gender, race, 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 MOP 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. A Sample Screening Log is available in the NIA Investigator’s Toolbox.

Note: This information is usually part of the reporting requirements for data and safety monitoring.

**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:**

Example of a screening log which includes Screening ID, Screened by, Age, Gender, Race/Ethnicity, Screen date and Eligibility Status

**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?**
   1. Who is responsible for reviewing/approving changes?
   2. What is the naming convention for the file?
   3. Where is the file kept so that the study team may access it and previous versions?
4. **Data entry:**
   1. Who is responsible?
   2. What system is used for data entry?
   3. Where are entered logs stored? How are they denoted?

## 7.3 Eligibility Criteria

Study eligibility is determined by a set of specific inclusion and exclusion criteria that are outlined in the study protocol. Potential participants must meet all entry criteria, and not meet any of the exclusion criteria, prior to treatment assignment. This section of the MOP describes 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.***

# 8.0 Study Intervention

This section of the MOP 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.

The intervention must be thoroughly described so that all participants have the same exposure:

* For **Pharmaceutical** studies, including drug, vitamin or other supplement, biological, nutritional and hormonal 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.](https://www.fda.gov/media/93884/download)
  + The MOP should describe how the investigational agent is to be stored, prepared, dispensed, and returned or destroyed. It should also provide instructions for completing drug accountability and administrative records.

**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>

**Behavior** and **life style** studies require a detailed description of how the intervention is to be carried out as well as documentation of the process.

**Procedure studies** (e.g., surgery) require a detailed description of the procedure.

***Sample Text:***

***The study intervention for Effects of Instructor-Led Exercises on Improved Osteoporosis Outcomes is an experimental set of exercises. This lifestyle 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 two 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 the participant at each visit and discuss any instances of discomfort.***

# 9.0 Randomization

This section of the MOP describes the randomization approach and procedures, including:

* ***Randomization Plan:*** The method used for generating randomization codes for assigning participants into treatment groups are describe in detail.
* ***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:***  At each site, the individual who is responsible for initiating the randomization procedure must be identified. This individual must know who 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 blinded randomization code in an automated, computerized log that is separate from the study data while other studies maintain the assignment in a paper-based 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 MOP 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 MOP 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 1st of the month of the next quarter. Each version received will be stored in the study binder.***

# 10.0 Blinding and Unblinding (Masking and Unmasking)

The Investigators’ procedures for unblinding should be described in detail in the MOP.

In most studies with randomization, participants and the treating physician are "blinded" or "masked" to the treatment and do not know if the participant is receiving the experimental or control intervention. In some instances, the study statistician and/or a designated study staff member may securely maintain the randomization codes so that the treatment assignments are not revealed. Randomization and blinding/unblinding procedures must be determined prior to the enrollment of the first participant*.* The MOP should clearly state who has access to masked and/or unmasked data on the study team. Additionally, the handling of the masked data, including the 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.***

Unblinding is a serious action and should be limited to reduce potential bias and maintain the integrity of the data. In the event that unblinding occurs, the following should be recorded:

* The ID of the unblinded participant,
* The reason for unblinding,
* The study staff person responsible for unblinding
* A list of person(s) who have been unblinded.

**11.0** **Study Measurements and Procedures**

Once a participant is enrolled in the study, there are typically baseline and follow-up assessments. To ensure that assessments and measures are conducted consistently across study participants, this section describes procedures for performing assessments and outcome measures. 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).

For example, in a weight loss study, the procedure for capturing weight might be described as follows:

Weigh participant between 7:00 am and 9:00 am while fasting and without shoes.

Blood pressure measurement – measure while participant is in a sitting position.

All outcome and safety evaluations (e.g., blood chemistries) should be delineated in this section.

**11.1 Timeline and visit schedul*e***

A useful study tool included in the MOP 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 MOP.

**Sample schedule:**

| *Assessment* | *Screening: Visit (Day-14 to*  *Day -1)* | *Baseline, Enrollment, Randomization: Visit 1 (Day 0)* | *Treatment Visit 2*  *Day 7*  *(±2 Days)* | *Treatment Visit 3*  *Day 14*  *(±2 Days)* | *Treatment Visit 4*  *Day 21*  *(±2 Days)* |
| --- | --- | --- | --- | --- | --- |
| *Informed Consent Form* | *X* |  |  |  |  |
| *Demographics* | ***X*** |  |  |  |  |
| *DXA* | ***X*** |  |  |  |  |
| *Medical History* | ***X*** |  |  |  |  |
| *General Physical Examination* | ***X*** | ***X*** | ***X*** |  |  |
| *Current Medications* | ***X*** | ***X*** |  |  |  |
| *Blood Chemistries* | ***X*** | ***X*** | ***X*** |  |  |
| *Hematology* | ***X*** | ***X*** | ***X*** |  |  |
| *Urine Analysis* | ***X*** | ***X*** | ***X*** |  |  |
| *Vital Signs* | ***X*** | ***X*** | ***X*** | ***X*** | ***X*** |
| *Inclusion/Exclusion Criteria* |  | ***X*** |  |  |  |
| *Enrollment/Randomization* |  | ***X*** |  |  |  |
| *Treatment Administration Form* |  |  | ***X*** | ***X*** | ***X*** |

**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 MOP, 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 provided for all study procedures. This may include defining the purpose of the assessment, the time of data collection, or the processes for handling unscheduled visits.

**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.***

**11.4 Final Study/Early Discontinuation Evaluations**

Evaluations for the final study/early discontinuation visit should be described in this section.

Participants should be actively followed through all study visits until the final visit.

It is important to note that if a study participant is discontinued from treatment, they should still be followed to the end of the study.

**12.0** **Concomitant Medications**

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

**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 the course of the study if the participant has been on stable dose 30 days prior to the screening visit:***

* ***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 MOP. The form/log should be included as an appendix.

The MOP provides a rationale for the concomitant medications that are required and restricted in the protocol. Please list all required and/or excluded concomitant medications in this section.

# 13.0 Safety Reporting

This section of the MOP details the definitions of and procedures for reporting adverse events and serious adverse events, as applicable. The [Data and Safety Monitoring Guidance for Investigators](https://www.nia.nih.gov/research/grants-funding/nia-guidance-clinical-trials#dsm) and [Events Process Flow](https://www.nia.nih.gov/research/clinical-research-study-investigators-toolbox#safety) should be used when developing this section.

The Guidelines provide:

* Definitions of adverse events, serious adverse events and unanticipated problems
* Responsibilities of NIA and investigators
* Reporting processes
* Description of terms used in reporting

Additionally, [template reporting forms](https://www.nia.nih.gov/research/clinical-research-study-investigators-toolbox#forms) are available for Adverse Events and Serious Adverse Events.

**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 MOP, 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 NIA 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 X.***
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. 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 located in the Investigator’s Toolbox. AEs and/or laboratory abnormalities identified in the protocol as critical to participant safety must be reported to the NIA 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](https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html) 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 MOP 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. 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 MOP, a plan for SAE reporting to the NIA 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 MOP. An example is available in the Investigator’s Toolbox.

All *unexpected*, serious adverse events (SAEs), unless otherwise specified in the protocol and approved by the IRB and the NIA, require expedited reporting by the Principal Investigator to the study's safety monitoring bodies and the NIA. Unexpected SAEs must be reported to the independent safety monitoring body and the NIA, 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 NIA and the independent monitoring body, are the responsibility of the Investigator(s) and should be described in this section.]

**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 X.***
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. 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 Study Compliance

This section should describe what constitutes a protocol deviation and process for reporting deviations to appropriate parties, including the NIA, site investigator, and the DSMB or Safety Officer. Please note, only protocol deviations that impact participant safety should be reported within 24 hours of occurrence if possible, or as soon as they are discovered. All other deviations should be reported routinely to the independent safety monitoring body. Investigators need to follow their IRB requirements for reporting protocol deviations to the Board. In addition, if monitors discover any of these deviations during a site visit, they should list any such occurrence in their monitoring report. The site study coordinator should maintain a log of all protocol deviations. A log for recording protocol deviations should also be in the appendix.

The study should adhere to IRB policies for reporting protocol deviations/violations. In addition, the reporting of deviations/violations should be discussed with the NIA 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 NIA 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
* Failure to obtain Informed Consent
* Visits or procedures conducted outside of the protocol specified window
* Failure to keep IRB approval up-to-date
* Wrong treatment administered to participant
* Follow-up visit at a time point different from that specified in the protocol

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 B** and should be included as an appendix of the MOP.

See [Protocol Deviations Form Template](https://www.nia.nih.gov/research/clinical-research-study-investigators-toolbox#forms).

# 15.0 Data Collection and Study Forms

This section of the MOP describes 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 MOP, please provide:

**Sample Text:**

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

1. ***Standard Satisfaction Discussion Inventory and Inquiry (SSDII)***
   1. Developed in 2006 to gauge satisfaction with treatment in patients with spinal issues (Dennis, 2006). 12 Items, Likert Scale. Delivered at each visit.
   2. See: Appendix Item 27
   3. Saved in G:Forms/Assessments/SSDII.pdf
   4. Previous Versions in G:Forms/Assessments/SSDII Past/
      1. Naming Convention: SSDII\_DDMMMYYYY\_StaffName.doc/pdf
      2. Responsible for Editing: Any Study Member
      3. Responsible for Updating/Approving: Study Coordinator
   5. Forms reviewed at monthly team meeting, study team member assigned by department head to edit as needed and submit to study coordinator.
   6. 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

## 15.1 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 describes how participant data are maintained in the study. All essential study documents must be retained by the investigator in a Participant Binder and generally include the following:

* Source documents (e.g., lab reports, x-rays, etc.)
* Signed informed consent forms
* Questionnaires completed by the participant
* Case Report Forms (CRFs)
* Data correction forms
* Diaries

***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**
* **Diaries**
* **Questionnaires completed by the participant**

## 15.2 Study Forms

In this section of the MOP, the following should be provided:

* List and description of study forms and their collection schedule
* Forms maintenance

For your reference, [Study Form templates](http://www.nia.nih.gov/research/dgcg/clinical-research-study-investigators-toolbox/study-forms) are available in the NIA Toolbox.

## 15.3 General Instructions for Completing Forms

In this section, if paper CRFs are used in the study, please provide a set of instructions for completing the CRFs to ensure quality and consistency in data collection. A set of guidelines for incomplete or illegible forms must be included. 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 single 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 not done, write ND and provide a reason.
  + If the information is not available, but the evaluation was done, write NAV.

***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 not applicable, write NA.
* ***Incomplete or Illegible forms: Incomplete forms that do not have adequate explanation (as described above) compromise the integrity of the entire study.***

## 15.4 Data Flow

This section of the MOP describes data flow, data entry, and data correction procedures. Specifically describe how the team will ensure that all forms are complete, intact, and transmitted to the data manager or how the data are directly entered into an electronic CRF (eCRF). This section should also provide a detail description of the handling of error identification and resolution, identification of useful reports, and deriving a frozen, analytic database from edited or "clean" records.

## 15.5 Administrative Forms

Administrative forms provide documentation of study processes and assist with study operations (e.g., screening log). In this section of the MOP, 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.

For additional examples of administrative forms, please see **Appendix C**.

## 15.6 Retention of Study Documentation

The length of time all study files are to be maintained should be specified in this section. NIH policy requires that studies conducted under a grant retain participant forms for three years and studies conducted under contract retain participant forms for seven years. Details about the federal policies surrounding record retention and access can be found at [2 CFR Part 215](http://www.whitehouse.gov/sites/default/files/omb/assets/omb/circulars/a110/2cfr215-0.pdf). Individual IRBs, institutions, 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. Additionally, for select studies that must meet FDA requirements, informed consent forms be retained for two years after a marketing application is approved for a product or, if an application is not approved, until two years after shipment and delivery of the product is discontinued for investigational use and the FDA is notified.

**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.**

# 16.0 Data Management

This section of the MOP describes the computer system and data management approach that will be used to support the study and details how data are to be collected, entered (e.g., if eCRFs are used), edited or corrected. In some studies, this information will be documented in a separate document, the “Data Management Plan.” For studies that involve a large number of participants, the investigators may wish to consider a computerized approach for data collection. See [NIA’s Data Management Tips](https://www.nia.nih.gov/research/clinical-research-study-investigators-toolbox#forms) for additional details. Whether using a computerized approach or manual procedures, investigators are encouraged to utilize systems or procedures 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
* **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 and account for accrual, forms entered and completed, etc.
* **Statistical Analysis** – mechanism to transmit data to statistical analysis packages (e.g., SAS)

Investigators should involve staff or colleagues with data management experience to assist with the determination of the data flow, error identification and resolution, development of useful reports, and deriving a frozen, analytic database from edited or "clean" records. These areas should be discussed in this section.

A Users Guide may need to be developed as a separate document to aid the study staff with data management tasks.

Investigators should be aware that systems for studies that will be submitted to the FDA must be documented and validated. “[Guidance for electronic systems is found on the FDA Web site, Title 21 Code of Federal Regulations (21 CFR Part 11) Electronic Records; Electronic Signatures-Scope and Application](http://www.fda.gov/RegulatoryInformation/Guidances/ucm125067.htm)”

**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.***

## 16.1 External Data

External data refers to data sent to or collected at a study organizational component other than a clinical site (e.g., central laboratory, imaging facility, etc.) This section of the MOP 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 the comprehensive list in “[Protecting Personal Health Information in Research: Understanding the HIPAA Privacy Rule, NIH Publication 03-5388](http://privacyruleandresearch.nih.gov/pdf/HIPAA_Booklet_4-14-2003.pdf)”) 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?**

## 16.2 Quality Control Procedures

This section should detail the Quality Control plan and describe any training and certification procedures. It may include standard operating procedures (SOPs), data and forms checks, monitoring, routine reports, and correction procedures.

### 16.2.1 Standard Operating Procedures

Standard Operating Procedures (SOPs) which relate to conduct of clinical trials should be listed in this section of the MOP. Note: Printed SOPs should not be inserted in the MOP; 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

### 16.2.2 Data and Form Checks

Most studies use computerized systems that provide data edits as a form of quality control. This section of the MOP (or alternatively, the Data Management Plan) can provide a summary of the checks that will be implemented for data quality control. Data and form checks depend upon the complexity of the study. Data quality control checks may identify potential data anomalies such as:

* Missing data or forms
* Out-of-range or erroneous data
* Inconsistent and illogical dates over time
* Data inconsistency across forms and visits
* Not completing all fields of a "completed form" or no reason for missing data is provided

### 16.2.3 Site Monitoring

The following section should describe site monitoring which is separate from the data and safety monitoring activities described in *Section 17.0 Data and Safety Monitoring Activities*.

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

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.

The purposes of monitoring visits are to:

* Ensure the rights and safety of participants
* Confirm that the study is conducted in accordance with GCP guidelines
* Ensure maintenance of required documents
* Verify adherence to the protocol
* Monitor the quality of data collected
* Ensure accurate reporting and documentation of all AEs and unanticipated problems

During monitoring visits, the data recorded on CRFs are reviewed and verified against source documents to ensure:

* Informed consent has been obtained and documented in accordance with IRB/ FDA regulations
* The information recorded on the forms is complete and accurate
* There are no omissions in the reports of specific data elements
* Missing examinations are indicated on the forms
* Participant disposition when exiting the study is accurately recorded

Site investigators must ensure that the monitor has access to all study documents, including informed consent forms, intervention accountability records, and source

Once the site visit is complete, a site monitoring report is drafted to provide feedback regarding any problems or issues that may have been uncovered during the visit. The report should state the problems uncovered during the visit and describe recommendations to correct them. A timeline should be agreed upon and included in the report to ensure that the follow-up of the issues is completed and implemented into the study’s procedures.

# 17.0 Data and Safety Monitoring Activities

The roles and responsibilities of the entities monitoring participant safety and study quality are described in this section. All clinical trials supported by NIA must have a data and safety monitoring plan. The type of safety monitoring is determined by the size and/or nature of the study and is specified in the Notice of Grant Award. Small, single-site studies usually have a Safety Officer, while multi-center studies require an independent (of the study, investigators, and participating institutions) Data and Safety Monitoring Board (DSMB) that is advisory to the NIA Director. However, if a small, single site study is determined to pose a significant risk to participants, a DSMB may be required.

To assist in preparing a monitoring plan, visit the [Data and Safety Monitoring](http://www.nia.nih.gov/research/dgcg/clinical-research-study-investigators-toolbox/data-and-safety-monitoring) page of the NIA Toolbox.

## 17.1 Reports

In this section of the MOP, please discuss the types and frequency of the reports which will be prepared and the members of the study team who are responsible for their completion.

Once a study begins, routine reports prepared by the site or study statistician are an important quality control tool. Monthly reports may describe target and actual enrollment, individuals screened with reasons for screen failure, and participant disposition (enrolled, active, completed, discontinued treatment, and lost to follow-up). Monthly reports can also list or summarize AEs and SAEs. Administrative reports can list the forms completed, entered, and missing and/or erroneous data and forms. DSMB/Safety Officer and NIA will specify the type and frequency of reports it wishes to receive. Other reporting requirements (e.g., to the IRB of Record and other regulatory bodies) should also be described in this section.

**Sample Text:**

* **Enrollment Report** 
  + Delivered to Safety Officer within 7 days after 1st enrollment
  + Produced by Study Assistant

## 17.2 Study Completion and Close-Out 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 MOP 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.
* Assurance that the study records are maintained and any relevant study information reported to the NIA.
* 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 E**.

### 17.2.1 Participant Notification

In this section of the MOP, please include the 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.

### 17.2.2 Confidentiality Procedures

This section of the MOP will discuss the safeguards which have been put in place 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. Study staff should be instructed in their responsibilities regarding data safeguards and cautioned against the release of data to any unauthorized individuals, unless such a release is approved by the Principle Investigator and NIA and is not in violation of applicable Federal and state laws.

The following is a list of study participant confidentiality safeguards:

* ***Electronic files*** *–*Data identifying participantsthat 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 formsand retained in a secure location.
* ***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***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.

### 17.2.3 Publications

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

All NIH-funded clinical trials are expected to register and submit results information to [Clinicaltrials.gov](http://www.clinicaltrials.gov/), as per the “[NIH Policy on Dissemination of NIH-Funded Clinical Trial Information](https://grants.nih.gov/policy/clinical-trials/reporting/understanding/nih-policy.htm)” for competing applications and contract proposals submitted on or after January 18, 2017.

# 18.0 MOP Maintenance

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

The footer on each page of the MOP should include the PI’s last name, type of MOP, version number, date and page number e.g. “*Brown\_Multi Site MOP\_v 1.0 24Mar2017….Page 2 of 30*” to facilitate any changes and/or additions.

The MOP 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 MOP should be continuously reviewed by the Coordinating Center/study staff to ensure that the operating procedures described are accurate. If any procedures have been changed or modified, the MOP should be updated, and the revised document distributed, with instructions, for replacement in the MOP. See **Appendix D** for a sample versioning page.

# *SUMMARY*

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

# Appendix A - Sample Schedule of Events

| ***Assessment*** | ***Screening: Visit (Day-14 to Day -1)*** | ***Baseline, Enrollment, Randomization: Visit 1 (Day 0)*** | ***Treatment Visit 2***  ***Day 7 (±2 Days)*** | ***Treatment Visit 3***  ***Day 14 (±2 Days)*** | ***Treatment Visit 4***  ***Day 21 (±2 Days)*** | ***Treatment Visit 5***  ***Day 28(±2 Days)*** | ***Treatment Visit 6***  ***Day 35 (±2 Days)*** | ***Follow-up: Final Visit***  ***Day 70 (± 7 Days)*** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *Informed Consent Form* | ***X*** |  |  |  |  |  |  |  |
| *Demographics* | ***X*** |  |  |  |  |  |  | ***X*** |
| *DXA* | ***X*** |  |  |  |  |  |  | ***X*** |
| *Medical History* | ***X*** |  |  |  |  |  |  |  |
| *General Physical Examination* | ***X*** | ***X*** | ***X*** |  |  |  | ***X*** | ***X*** |
| *Current Medications* | ***X*** | ***X*** |  |  |  |  |  |  |
| *Blood Chemistries* | ***X*** | ***X*** | ***X*** |  |  | ***X*** |  | ***X*** |
| *Hematology* | ***X*** | ***X*** | ***X*** |  |  | ***X*** |  | ***X*** |
| *Urine Analysis* | ***X*** | ***X*** | ***X*** |  |  | ***X*** |  | ***X*** |
| *Vital Signs* | ***X*** | ***X*** | ***X*** | ***X*** | ***X*** | ***X*** | ***X*** | ***X*** |
| *Inclusion/Exclusion Criteria* |  | ***X*** |  |  |  |  |  |  |
| *Enrollment/Randomization* |  | ***X*** |  |  |  |  |  |  |
| *Treatment Administration Form* |  |  | ***X*** | ***X*** | ***X*** | ***X*** | ***X*** |  |
| *Concomitant Medications* |  | ***X*** | ***X*** | ***X*** | ***X*** | ***X*** | ***X*** | ***X*** |
| *Adverse Events* |  | ***X*** | ***X*** | ***X*** | ***X*** | ***X*** | ***X*** | ***X*** |

# Appendix B - Sample Protocol Deviation/Violation Log

Protocol Title:

Protocol Number:

Site: Principal Investigator:

| **Protocol Deviation/**  **Violation Code:** | **Participant Initials** | **Participant ID#** | **Date Deviation /**  **Violation Occurred:**  **mm/dd/yyyy** | **Date Protocol Deviation**  **/ Violation Form**  **Completed: mm/dd/yyyy** | **Contact Person**  **(if applicable)** |
| --- | --- | --- | --- | --- | --- |
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## SAMPLE PROTOCOL DEVIATION / VIOLATION CODES

***Consent Form:***

1. Missing or not obtained
2. Not signed and dated by participant
3. Does not contain all required signatures
4. Outdated, current IRB-approved version not used
5. Not protocol specific.
6. Does not include updates or information required by the IRB

***Randomization:***

1. Ineligible participant enrolled and/or randomized
2. Participant is randomized prior to determining whether eligible for study
3. Occurs outside protocol window

***IRB:***

1. Not reporting a serious complication within 24 hours
2. Approvals not kept up to date
3. Enrollment and/or treatment occurs prior to IRB approval or during period when “on hold”
4. Reportable serious adverse events not reported to IRB

***Participant:***

1. Receives wrong treatment
2. Visits occur outside expected follow-up window
3. Entered into another study

***Study Data and/or Forms:***

1. Missing data and/or forms
2. Missing radiology and/or operative reports
3. Forms or data not sent from clinical site to coordinating center

# Appendix C - Examples of Administrative Forms

An Administrative Form constitutes any form that would not be included in the study database. The following is a list of administrative forms that should be considered for a study. Given that each study is unique, forms could be omitted and/or added at the investigator’s discretion depending on the nature of the study.

* ***Screening and Enrollment Log* -** Used to list participants screened; includes those who fail screening and those who are enrolled.
* ***Training Log\**** **-** Documents study-specific training completed by staff exhibiting their qualifications to perform tasks involved in the clinical research study. Other training may also be listed on this log.

\*Forms could also be considered a regulatory document rather than an administrative form.

# Appendix D - Sample MOP Modification Log

**MOP MODIFICATION LOG**

| **Section #** | **Version #** | **Date Modified** | **Page #** | **Text Location** | **Brief Modification Summary** |
| --- | --- | --- | --- | --- | --- |
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# Appendix E - NIA Single-Site Clinical Trial Sample Closeout Procedures

## I. INTRODUCTION

### Purpose

The purpose of this document is to describe an orderly approach to the separation of participants

from a clinical trial and the administrative procedures associated with the trial’s completion.

### Types of Closeout

1. Scheduled - upon completion of the trial.
2. Unscheduled - as a result of failure to obtain continuation funding, negative or positive findings, findings in other studies that impact on the clinical trial, or other unforeseen events.

## II. SITE CLOSEOUT

The study site is responsible for ensuring the following activities are completed prior to study closeout along with the Participant Closeout Procedures described in Section III below.

1. Study Forms

* All outstanding Case Report Forms (CRFs) should be collected, organized, and corrections made, where necessary.
* All data queries should be corrected and resolved.

1. Safety Reporting

* All adverse events (both serious and non-serious) should be recorded and followed up to resolution in accordance with procedures detailed in the protocol.
* All serious adverse events (SAEs) should have been reported to the Data and Safety Monitoring Board (DSMB) or Safety Officer, Institute, Institutional Review Board (IRB), and other organizations, as specified in the protocol and Data and Safety Monitoring Plan (DSMP).
* All adverse events should have been reported as specified in the protocol.

1. Study Files

* The investigator’s study files should be complete and up to date with originals of the following maintained in the Study Binder, as relevant:
  + Investigator(s) Curriculum Vitae(s) (CVs), Licenses and Training Records
  + Package Insert(s), as relevant
  + IRB approval letters for the protocol, all amendments, Informed Consents, annual reviews and advertisements (including updated approvals)
  + IRB membership list
  + All IRB correspondence
  + Institute correspondence
  + Site signature log
  + Drug accountability records documenting the investigational product received, dispensed and returned or destroyed
  + Copy of randomization code for randomization, if applicable
* All informed consents should be signed and on file.
* Record retention procedures should be documented with respect to type and length of retention and consequences of improper record retention and should conform to protocol and institutional requirements. The site should be completely familiar with required record retention policies.

1. Clinical Supplies

* Clinical supplies, including any treatment intervention materials, must be shipped or disposed of according to protocol directions.
* As relevant, drug accountability records (shipping, receipt, dispensing, return or destruction) should be up to date.

1. Laboratory Records and Specimen Retention

* The site should ensure that the laboratory records are complete and up to date (reference ranges, laboratory certifications, specimen tracking records, specimen storage records).
* If specimens are to be stored, a plan should be in place to address issues such as specimen retention, use, and methods for protecting patient confidentiality. As relevant, study specimens should be transmitted to the analysis center, analyzed, results recorded for the study, and specimens stored with proper documentation.

1. Notifications and Equipment Removal

* A final report should be submitted to the IRB and should conform to institutional reporting requirements. The report is likely to include, but is not limited to, study conduct and outcome, pertinent safety and efficacy observations, complete disclosure of any SAEs experienced during the course of the study, and the study closeout date.
* As relevant, arrangements should be made for the removal and shipment of any study- specific equipment received by the site (e.g., computers, diagnostic equipment, and participant monitoring devices).

Figure 1 provides a sample study documentation list, and Figure 2 provides a sample Closeout

Checklist.

### Sample Study Documentation List

| **Document** | **Purpose** |
| --- | --- |
| Treatment intervention product(s) accountability at site | Documents that the treatment intervention product(s) have been used according to the protocol. Documents the final accounting of treatment product(s) received at site, dispensed to participants, returned by the participants, and returned or destroyed. |
| Final report by investigator to IRB, as required | To document completion of the trial |
| Final Trial Closeout  Monitoring Checklist, if relevant | To document that all activities required for trial closeout are completed, and copies of essential documents are held in the appropriate files |
| Audit Certificate (if relevant) | To document that audit was performed |

|  |
| --- |
| Sample Study Closeout Checklist Investigator has signed and dated all CRFs.  CRFs for all participants have been filed or transmitted as described in the Manual of Operating Procedures.  All appropriate documents are in the study files.  As relevant, study drug has been shipped or destroyed, as described in the study protocol and/or Manual of Operating Procedures.  The final study close-out report has been submitted to the IRB.  Documents are retained as specified in the Manual of Operating Procedures or IRB directives, whichever is longer.  There is a plan in place in the event of an audit by the NIA, as relevant.  Final report has been submitted to the NIA. |

## III. PARTICIPANT RIGHTS AND NOTIFICATION

The study site should prepare a letter that thanks each study participant. The letter should be circulated to each site for distribution. The letter may include but not be limited to the following information:

* Study findings
* Treatment assignment, as relevant
* Treatment options, as relevant, whether continued treatment with the assigned intervention is indicated, and how and where treatment may be obtained
* Transfer of care responsibilities
* Rights to confidentiality, privacy, and to no further contact from study staff, if that is participant’s preference
* Subsequent updates or recalls if new and important information emerges following separation
* Contact information of study staff

A copy of the letter should be included in the participant’s file.

## IV. INSTITUTE RESPONSIBILITIES

The NIA may wish to send staff or a Contractor to ensure that closeout procedures are appropriately conducted at any of the study sites.