**National Institute of Arthritis and
Musculoskeletal and Skin Diseases**

# Guidelines and Template for Developing a Multi-siteManual of Operating Procedures (MOP)

***December 2020***

# <Study Title>

*Enter the title of the study here. The title should be recognizable by administrative support study team, and sufficiently different from other protocol titles to avoid confusion.*

*If there is a “short title” (e.g., an abbreviation used to refer to the study title, include here and that can* *be used throughout this document in place of the full title).*

**Protocol Number: <Number, if available>**

**Study Principal Investigator: <Study Principal investigator, if applicable>**

**Site Investigator: <Site investigator>**

**Site Name: <Site name>**

**Grant/Contract Number: <Number, if available>**

**Funded by: <NIH Institute or Center (IC)>**

**Version Number: v.<x.x>**

**<Day Month Year>**

*All versions should have a version number and a date. Use the international date format (day month year) and write out the month (e.g., 23 June 2020).*

**Summary of Changes from Previous Version:**

| **Affected Section(s)** | **Summary of Revisions Made** | **Rationale** |
| --- | --- | --- |
|  |  |  |
|  |  |  |
|  |  |  |

## TABLE OF CONTENTS

[ABBREVIATION GLOSSARY 5](#_Toc57914433)

[INTRODUCTION 9](#_Toc57914434)

[HOW TO USE THIS DOCUMENT 9](#_Toc57914435)

[OVERVIEW 10](#_Toc57914436)

[MOP OUTLINE AND GUIDE 11](#_Toc57914437)

[1.0 Introduction 11](#_Toc57914438)

[2.0 STUDY OVERVIEW 12](#_Toc57914439)

[3.0 STUDY FLOW DIAGRAM 12](#_Toc57914440)

[4.0 STUDY TEAM ROSTER, ORGANIZATION AND RESPONSIBILITIES 14](#_Toc57914441)

[4.1 ORGANIZATION CHART 15](#_Toc57914442)

[4.2 TRAINING AND COMMUNICATIONS PLAN 16](#_Toc57914443)

[5.0 Recruitment and Retention Plan 16](#_Toc57914444)

[5.1 PARTICIPANT RECRUITMENT 16](#_Toc57914445)

[5.2 PARTICIPANT RETENTION 17](#_Toc57914446)

[6.0 Screening and Eligibility Criteria 18](#_Toc57914447)

[6.1 SCREENING 18](#_Toc57914448)

[6.2 SCREENING LOG 19](#_Toc57914449)

[6.3 ELIGIBILITY CRITERIA 20](#_Toc57914450)

[7.0 Informed Consent and HIPAA 21](#_Toc57914451)

[7.1 HIPAA AUTHORIZATION 22](#_Toc57914452)

[8.0 Study Intervention 23](#_Toc57914453)

[9.0 Randomization/Allocation and Participant Assignment 25](#_Toc57914454)

[9.1 INVESTIGATIONAL PRODUCT ACTIVITIES 26](#_Toc57914455)

[10.0 Masking and Unmasking 27](#_Toc57914456)

[11.1 STUDY VISIT SCHEDULE 28](#_Toc57914457)

[11.2 VISIT PROCEDURES 29](#_Toc57914458)

[11.3 FOLLOW-UP 30](#_Toc57914459)

[12.0 Concomitant Medications 30](#_Toc57914460)

[13.0 Safety Reporting 31](#_Toc57914461)

[13.1. ADVERSE EVENT(AE), SERIOUS ADVERSE EVENT(SAE), AND UNANTICIPATED PROBLEM (UP) DEFINITIONS 31](#_Toc57914462)

[13.2 ADVERSE EVENT REPORTING 32](#_Toc57914463)

[13.3 SERIOUS ADVERSE EVENT REPORTING 33](#_Toc57914465)

[13.4 UNANTICIPATED PROBLEMS REPORTING 34](#_Toc57914466)

[14.0 Data and Safety Monitoring Activities 35](#_Toc57914467)

[15.0 Study Compliance 35](#_Toc57914468)

[16.0 Data Collection and Study Forms 36](#_Toc57914469)

[16.1 SOURCE DOCUMENTATION 37](#_Toc57914471)

[16.2 GENERAL INSTRUCTIONS FOR COMPLETING FORMS 38](#_Toc57914472)

[16.3 RETENTION OF STUDY DOCUMENTATION 39](#_Toc57914473)

[16.4 ADMINISTRATIVE FORMS 40](#_Toc57914474)

[17.0 Data Management 40](#_Toc57914475)

[17.1 EXTERNAL DATA 41](#_Toc57914476)

[17.2 QUALITY CONTROL PROCEDURES 41](#_Toc57914477)

[17.2.1 STANDARD OPERATING PROCEDURES 41](#_Toc57914478)

[17.2.2 DATA AND FORM CHECKS 41](#_Toc57914479)

[17.2.3 CLINICAL SITE MONITORING 42](#_Toc57914480)

[18.0 Reports 42](#_Toc57914481)

[19.0 Study Completion and Closeout Procedures 43](#_Toc57914482)

[19.1 PARITICPANT NOTIFICATION 43](#_Toc57914483)

[20.0 Policies 43](#_Toc57914484)

[20.1 CONFIDENTIALITY PROCEDURES 43](#_Toc57914485)

[20.2 PUBLICATIONS 44](#_Toc57914486)

[21.0 MOP Maintenance 45](#_Toc57914487)

[SUMMARY 45](#_Toc57914488)

## FIGURES & TABLE

[FIGURE 1: SAMPLE STUDY DIAGRAM 13](#_Toc57977267)

[TABLE 1: SAMPLE STUDY TEAM ROSTER 14](#_Toc57977268)

[FIGURE 2: ORGANIZATION CHART 15](#_FIGURE_2:_ORGANIZATION)

## APPENDICES

APPENDIX A:SAMPLE ADVERSE EVENT FORM

APPENDIX B: SAMPLE SERIOUS ADVERSE EVENT FORM

APPENDIX C: SAMPLE UNANTICIPATED PROBLEM FORM

APPENDIX D: SAMPLE PROTOCOL DEVIATION LOG

APPENDIX E: SAMPLE INFORMED CONSENT PROCESS CHECKLIST

APPENDIX F: SAMPLE ELIGIBILITY CHECKLIST

APPENDIX G: SAMPLE CASE REPORT FORMS

(*Please note this appendix should include all study forms with a cover page listing out the forms that are included; sample templates for the five forms listed below are available on the NIAMS website for your reference*)

APPENDIX G-1: DEMOGRAPHICS FORM

APPENDIX G-2: MEDICAL HISTORY FORM

APPENDIX G-3: PRIOR AND CONCOMITANT MEDICATIONS FORM

APPENDIX G-4: VITAL SIGNS FORM

APPENDIX G-5: STUDY DISPOSITION FORM

APPENDIX H: SAMPLE CLINICAL TRIAL CLOSEOUT PROCEDURES (MULTI-SITE)

## ABBREVIATION GLOSSARY

***Adverse Event (AE) –*** Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research.

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

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

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

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

***Data and Safety Monitoring Plan (DSMP) –*** A plan that outlines the data and safety monitoring oversight of a clinical trial.

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

***Good Clinical Practice (GCP) –*** E6 GCP from the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use provides guidance for good design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials to ensure data and results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

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

***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.

***Investigator Brochure (IB) –*** 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.

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

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

***Manual of Operating Procedures (MOP)* *–*** A “cookbook” 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.

***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 abbreviation ND should be used to fill out the field.

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

***Office for Human Research Protection (OHRP) –*** A federal government agency within the Department of Health and Human Services (DHHS) charged with the protection of human subjects participating in government-supported research. The OHRP issues assurances to institutions reviewing human subjects research and oversees compliance of regulatory guidelines by research institutions.

***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 team, 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, multi-site clinical studies. The SO advises the NIAMS Program Director regarding participant safety, scientific integrity and ethical conduct of a study.

***Serious Adverse Event (SAE) –*** Any adverse event temporally associated with the subject’s participation in research that meets any of the following criteria:

1. results in death;

2. is life-threatening (places the subject at immediate risk of death from the event as it occurred);

3. requires inpatient hospitalization or prolongation of existing hospitalization;

4. results in a persistent or significant disability/incapacity;

5. results in a congenital anomaly/birth defect; or

6. any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

***Site Investigator*** – The individual with primary responsibility for achieving the technical success of the project at the site, while in close communication with the study Principal Investigator and in compliance with the financial rules and requirements, administrative policies, and regulations associated with a grant award. Although site investigators may have a study team to assist them with the management of the project, the ultimate responsibility for study oversight rests with the site investigator.

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

***Study Coordinator –*** An individual at a study site 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.

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

***Unanticipated Problem (UP) –*** 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.

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

## INTRODUCTION

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH) has an obligation to ensure grantees it supports conducting clinical research are compliant with Federal laws and regulations, including all applicable NIAMS/NIH policies and guidelines to protect the safety of all research participants. When preparing to implement a study, the study Principal Investigator (PI) and site investigator(s) must be aware of the terms and conditions of the award outlined in their Notice of Award, with respect to required training, data and safety monitoring oversight, registration and reporting of research results, and all applicable regulatory approvals, including but not limited to, Institutional Review Board (IRB).

The purpose of this document is to assist investigators of multi-site studies in the development of a study Manual of Operating Procedures (MOP), by providing them with guidelines and template to follow. A multi-site study is defined as a single protocol involving more than one clinic (i.e., performance site) and one or more centers (e.g., Data Coordinating Center (DCC)) to receive and process data. The performance site and Coordinating Center (CC) may or may not be in the same location. The role of the MOP is to facilitate consistency in study implementation and data collection across study visits, participants, and sites. Use of the MOP increases the likelihood that study implementation will be consistent, data quality and integrity will be high, participant safety will be protected, and results will be scientifically valid. The NIAMS website lists many links and references to helpful policies, guidelines, and templates related to clinical research (see <https://www.niams.nih.gov/>). All study team members participating in the conduct of this study at participating institutions should have access to the MOP guidelines and template and be familiar with its contents.

## HOW TO USE THIS DOCUMENT

This is a guidance and template document to be used by investigators developing a MOP for clinical studies supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases. 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 study, there is no need to include it. Refer to the *MOP Outline and Guide* on page 9 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 sample text verbatim.**

## OVERVIEW

A MOP is for clinical interventional trials (e.g., drug, surgery, behavioral, device, etc.), but may also be useful for other types of clinical research studies. The MOP transforms the study protocol into a handbook for the study team. Its purpose is to provide the operational detail to ensure that study procedures are carried out consistently. The study team (investigators, coordinators, statisticians, etc.) develops the MOP and submits it to the NIAMS for review and approval before the study can commence.

During a study's planning phase, the investigators and their institutional colleagues delineate the protocol. The protocol must be approved by the IRBs of all clinical site institutions participating in the study.

MOP development requires complete versions of a final protocol, study forms (often called case report forms [CRFs]), Investigator Brochure (IB) or Device Manual, if applicable, and Informed Consent Form (ICF)/Assent Form. The timeline for development of study materials must be planned for and typically takes several months.

Development of the MOP requires the involvement of the investigator and study team to ensure the guidelines are written to accurately reflect how the study procedures will be performed. In multi-site clinical studies, a Steering Committee or other designated internal Advisory Committee, comprised of the investigators from each of the sites, can be appointed to finalize the protocol and elements of the MOP before it is sent to the NIAMS.

The MOP is a dynamic document that must be updated throughout the life of the study to reflect any protocol or ICF 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 referenced and updated, such as a three-hole binder or electronic format. Each page of 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. Older versions of 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 NIAMS 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. If a section is not relevant to the study (e.g., randomization in a study with no randomization), it should not be included in the MOP.

## MOP OUTLINE AND GUIDE

### 1.0 Introduction

The MOP submitted to the NIAMS should include all the elements listed below, if relevant. Please consider adding a table of contents and a glossary of terms at the beginning of the document and ensure that all abbreviations found within the document are defined upon first use. The NIH-FDA approved protocol template for FDA regulated Phase 2 or 3 studies is available to guide you in writing your study protocol. Please visit Clinical Trials at: <http://osp.od.nih.gov/office-clinical-research-and-bioethics-policy/clinical-research-policy/clinical-trials>. This link also includes a protocol template for the behavioral and social sciences clinical trials under *Clinical Trial E-Protocol Tool and Template Documents*. Additionally, there is an electronic protocol writing tool that aims to facilitate the development of phase 2 and 3 clinical trial protocols that require a Food and Drug Administration (FDA) Investigational New Drug (IND) or Investigational Device Exemption (IDE) Application: <https://e-protocol.od.nih.gov/#/home>. Use of this template is highly encouraged.

1. Study Overview
2. Study Flow Diagram
3. Study Team Roster, Organization, and Responsibilities
4. Recruitment and Retention Plan
5. Screening and Eligibility Criteria
6. Informed Consent and HIPAA Process
7. Study Intervention
8. Randomization/Allocation and Participant Assignment
9. Masking and Unmasking
10. Study Visit Schedule and Procedures
11. Concomitant Medications
12. Safety Reporting
13. Data and Safety Monitoring Activities
14. Study Compliance
15. Data Collection and Study Forms
16. Data Management
17. Reports
18. Study Completion and Close-Out Procedures
19. Policies
20. MOP Maintenance

### 2.0 Study Overview

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

***Sample Text:***

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

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

**Checklist:**

* **Study Type and Phase**
* **Study Population (i.e. sample size, participant demographics and condition)**
* **Study Design (e.g. objectives, intervention, endpoints, etc.)**

### 3.0 Study Flow Diagram

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

# FIGURE 1: SAMPLE STUDY DIAGRAM

 

### 4.0 Study Team Roster, Organization and Responsibilities

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

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

***Sample Text:***

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

TABLE 1: SAMPLE STUDY TEAM 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 (e.g., IRB or FDA*
* *Quality control procedures*
* *Ensuring compliance with human subjects regulations and policies*
 |
| *Mary Smith* | *City Hospital**Research Department**123 Brown Street**Suite 535 B* *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 MOP and study forms*
* *Maintenance of the study binder (regulatory and study documents)*
* *Retaining specific records, (e.g., laboratory or drug distribution records)*
 |

**Roles Checklist**

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

**Responsibilities Checklist:**

* **Records and files maintenance**
* **Serving as contact to and submitting files to IRB/HRPO**
* **Training study team on study procedures**
* **Data collection**
* **Participant identification**
* **Participant screening**
* **Participant enrollment**
* **Participant retention**
* **Data entry**
* **[insert responsibilities as required by protocol]**

###

#### 4.1 Organization Chart

This section of the MOP should include the study organization chart. It is a diagram that shows the structure of the study and the relationships among the study team members. Please see an example below, but consider all groups and teams involved in your study as the flow of reporting may differ.

FIGURE 2: SAMPLE ORGANIZATION CHART



#### 4.2 Training and Communications Plan

This section should detail a plan for initial training of the study team members at all the sites on the study, subsequent training of any new study team members as they join the study and any re-training of study team required as a result of modifications to the study protocol. The plan for ensuring GCP and Human Subjects Protection Training should also be detailed in this section.

The communication plan between the CC and the sites, including but not limited to whether/how often calls will be held, who will be involved in these calls, and how often the sites will need to provide screening/enrollment information to the CC should be described in this section.

***Sample Text:***

***To ensure adherence to the study protocol and high data quality, there will be a variety of different trainings (include specificity). All study team members will initially be trained on the study through an initial investigator meeting, and this training will be documented on a training log that is signed by all attendees and filed in the regulatory binder. Site training will be required for any new study team member who joins the study team. In instances of protocol compliance issues, the study team will be retrained. All training/retraining will be documented on a training log and filed in the regulatory binder.***

***The study PI and the Project Manager /Lead Coordinator at the Coordinating Center (CC) will maintain primary responsibility for regular communications among all clinical sites throughout the implementation of the trial to ensure efficient and consistent operations. A monthly coordinator call will be led by the CC Project Manager and attended by the coordinators at all of the clinical sites. The Project Manager will draft an agenda and follow the call with minutes and action items documenting the discussion. The study PI will reach out to the site investigators as needed should issues occur and remain available should the site investigators need to reach out with any issues. A newsletter will also be distributed on a monthly basis tracking enrollment across sites, sharing any study news and addressing any frequently asked questions (FAQs). The site investigator will meet internally with his study team members including data management on a weekly basis to ensure the study is progressing as planned.***

### 5.0 Recruitment and Retention Plan

#### 5.1 Participant Recruitment

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

 ***Sample Text:***

***The site investigator and/or Study Coordinator will pre-screen potential participants referred by Dr. Brown, a treating Rheumatologist in the Arthritis and Musculoskeletal Clinic at the University Hospital. The site investigator will present the study information to the potential participants during a routine clinic visit. If the participant is interested and willing to consent immediately, the site investigator 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 in 1-week to learn if he/she is still interested and would like to participate. If potential participant is still interested, a screening visit will be scheduled to review the ICF and 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 potential participants approached?**
	+ **Be specific: “Approach the potential participant in their hospital room during nurse blood draws.”**
* **Are the participants recruited through marketing materials, such as a poster?**
	+ **Are they instructed to call a number? If so, are they to leave a message, set up an appointment, or something else?**

#### 5.2 Participant Retention

This section of the MOP should describe the plan for participant retention, as well as an action plan or corrective action plan in case there are problems with retention. The follow-up process should clearly specify how many times participants who do not appear for their visits will be contacted, at what time intervals (e.g., every 2 weeks, monthly, etc.), via what method (e.g., phone, email, letter, family members), and also at what point a participant would be considered lost to follow up and no further contact attempts will be made.

***Sample Text:***

***Every effort will be made by the site investigator 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 a questions and answer sessions after each visit, if needed.***
* ***Distributing newsletters to participants to provide feedback information on the status of the study***
* ***Assessing each participant’s drop-out potential and intervening as needed to keep participants interested in continuing to participate***

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

**Participant Retention Checklist:**

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

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

### 6.0 Screening and Eligibility Criteria

#### 6.1 Screening

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

***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. ***The Study Coordinator will take the participant’s phone call and explain the study. If participant is interested, and meets eligibility criteria as outlined in Section 6.3, the Study Coordinator will set up a screening appointment.***
	3. ***If the participant leaves a message, the Study Coordinator will return their call and explain the study. If participant is interested, and meets eligibility criteria as outlined in Section 6.3, the Study Coordinator will set up a screening appointment.***
2. ***Screening Phase***
	1. ***The Study Coordinator will meet with potential participant to explain the study***
	2. ***The Study Coordinator will ensure that potential participant meets eligibility criteria as outlined in Section 6.3***
	3. ***The Study Coordinator will probe potential participant’s ability to complete the duration of the study:***
		1. ***Is the participant planning to move during the time they will be in 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. ***The Study Coordinator will have the participant sign an Informed Consent Form, HIPAA Authorization Form, and provide copies to the participant while placing originals in participant’s study file.***
	5. ***The Study Coordinator will collect contact information, including contact information for one family member and one friend.***

#### 6.2 Screening Log

A Screening Log documents all individuals evaluated for study eligibility. It generally contains the individual’s study identification number (screening number), age, sex, date screened, date of consent, eligibility for enrollment, and ineligible for study participation 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. (Note: this information is usually part of the reporting requirements in the data and safety monitoring plan.)

**Screening Log Checklist:**

* **Consult protocol for necessary data fields for screening log, including:**
	+ **Screening/participant ID**
	+ **Screening member of Study Team**
	+ **Date of consent**
	+ **Date screened**
	+ **Identifying characteristics (Demographics)**
	+ **Eligibility status**

**Sample Screening Log:**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Screening/ participant ID** | **Initials of Person Conducting Screening** | **Date Consented** | **Date Screened** | **Ethnicity** | **Race** | **Sex** | **Age** | **Eligibility Status** |
| T001 | JD | 21/Dec/2019 | 22/Dec/2019 | Hispanic/Latino  | Black/ African American | F | 71 | Eligible; Declined |
| T002 | JD | 28/Dec/2019 | 03/Jan/2020 | Not Hispanic/Latino | White | M | 66 | Eligible; Enrolled on 03/Jan/2020 |
| T003 | RA | 01/Jan/2020 | 08/Jan/2020 | Not Hispanic/Latino | Asian | M | 59 | Not Eligible; Exclusion criteria #4 |
| T004 | JD | 01/Jan/2020 | 09/Jan/2020 | Hispanic/Latino | White | M | 62 | Eligible; Enrolled on 09/Jan/2020 |

**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 saved?**
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?**

#### 6.3 Eligibility Criteria

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

A sample Eligibility Checklist form is shown in **Appendix F**.

***Sample Text:***

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

***Inclusion Criteria***

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

***Exclusion Criteria***

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

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

### 7.0 Informed Consent and HIPAA

This section of the MOP should describe the specific instructions for obtaining informed consent. If there are multiple consent documents (i.e. 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 of the person who will discuss the nature of the study with the potential participant and sign the consent form
* Will the potential participant be given sufficient time to review the consent form; and a description of what procedure would be followed if the potential participant needed additional time to review the consent form (i.e. additional time provided at the first meeting time on site, take consent document home and return; when returned, how returned [e-mail, fax, in-person])
* When a copy of the signed consent will be given to the individual and where the original signed copy of the consent will be stored
* Re-consent process if participants need to be re-consented at any time during the study.

In addition, the informed consent form should include the following mandatory ClinicalTrials.gov inclusion statement required by law: "A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time."

The IRB-approved Informed Consent Form should be included as an appendix to 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) and [OHRP Informed Consent Checklist](https://www.hhs.gov/ohrp/regulations-and-policy/guidance/checklists/index.html).

Furthermore, for all clinical trials conducted or supported by a Federal department or agency, sections 46.102(b) and 46.116(h) of the [Revised Common Rule](https://www.ecfr.gov/cgi-bin/text-idx?SID=300df04ebff09c7b23735d902a3f645a&mc=true&tpl=/ecfrbrowse/Title45/45cfr46_main_02.tpl) requires the posting of an IRB-approved consent form on one of the designated public federal websites. The form must be posted after recruitment closes, and no later than 60 days after the last study visit. For further details on this policy, please see [Posting Clinical Trial Informed Consent Forms.](https://grants.nih.gov/policy/clinical-trials/informedconsent.htm)

It is highly recommended that the study team utilize a checklist to document the consenting process. A sample Informed Consent Process Checklist is shown in **Appendix E**.

***Sample Text:***

* ***Study Informed Consent Form: General description of the study and participant’s responsibilities – page 34, Appendix Item E***
	+ ***Administered by the Study Coordinator at Scheduled Screening Visit at C.F. Memorial Hospital, Suite 535B***
	+ ***The Study Coordinator explains risks and benefits, reminding study participation is voluntary, and may discontinue at any time (and procedure for termination)***
	+ ***The Study Coordinator provides contact information in case of medical emergency due to study participation, or for questions about participant rights***
	+ ***The Study Coordinator explains who has access to participant’s protected health information, and how confidentiality is maintained***
	+ ***The Study Coordinator explains any costs participation may incur***
	+ ***The Study 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 the participant, and placed in his or her file***

#### 7.1 HIPAA Authorization

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

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

The format of the HIPAA authorization is dictated by the local IRB, meaning that it can be a separate document from the ICF, reviewed and signed by the participant in addition to reviewing and signing the ICF. Investigators should review information provided in Impact of the HIPAA Privacy Rule on NIH Processes Involving the Review, Funding, and Progress Monitoring of Grants, Cooperative Agreements, and Research Contracts at <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html> and Protecting Personal Health Information in Research: Understanding the HIPAA Privacy Rule at <http://privacyruleandresearch.nih.gov/pdf/HIPAA_Booklet_4-14-2003.pdf>.

***Sample Text:***

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

**HIPAA Checklist**:

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

* **Name**
* **Date of Birth/Age**
* **Home address, including zip code**
* **Phone number(s)**
* **Qualifying medical condition for inclusion into the clinical research study**

### 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 study protocol.

A study intervention is defined as a manipulation of the participant’s environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples of interventions include drug/molecule/compound, supplement, biologic, gene transfer, vaccine, device, procedure (e.g., surgical technique), strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise), treatment strategies, prevention strategies, and diagnostic strategies. A clinical trial has an intervention that may be assessed for safety, efficacy, or effectiveness. Many clinical trials are mechanistic or exploratory and fall outside the realm of efficacy and effectiveness trials.

**Types of Examples:**

**For drug, vitamin, or other supplement, biologic, gene transfer, and vaccine intervention studies**, the distribution, preparation and handling, labeling, and administration are detailed along with the duration of the intervention and criteria for 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, 2019 <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRsearch.cfm?CFRPart=312>. This section must include the regulatory approval status of the drug, whether it is a new indication/population or approved for the disease/condition under study. A detailed description of the information that must be provided is documented in the ICH E6 Guideline for Good Clinical Practice. This document is available on the Internet at <https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf>

**Device studies** require a detailed description of the device and its intended use. This section must include the regulatory approval status of the device, and whether it has an investigational device exemption. Information on device studies is provided in the Code of Federal Regulations (CFR) Title 21, Part 812, revised as of April 1, 2019, at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=812&showFR=1>

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

**Behavior** **and** **lifestyle** **studies** require a detailed description of the intervention as well as documentation of the process. For more details, please refer to the intervention monitoring manual here.

***Sample Text:***

***This study is an NIH defined phase III clinical trial with three arms. The study interventions are Cognitive Behavioral Therapy (CBT), Home Exercise, and Physical Therapy (PT). A summary of the three interventions is given below. Further explanation of each intervention and its key components follows.***

| ***Arm***  | ***CBT*** | ***Home Exercise*** | ***PT*** |
| --- | --- | --- | --- |
| ***Arm 1***  | ***✓***  |  |  |
| ***Arm 2***  | ***✓***  | ***✓***  |  |
| ***Arm 3***  | ***✓***  | ***✓***  | ***✓***  |

***During the active intervention phase (weeks 1-8), each intervention consists of 16 in-person sessions held twice per week over 8 weeks. Sessions last 90 minutes and will be led by either a physical therapist or clinical psychologist (depending on the study arm) using manualized protocols.***

***During the maintenance phase (4 additional sessions over a 7-month follow up period), the first follow-up session will be held 4-weeks after the end of the intervention and then at 2-month intervals until the final assessment. Sessions will be conducted by the same interventionists and will follow the protocols for Home Exercise, CBT, or PT based on participants’ original assignment.***

***A description of the content of each intervention is summarized in Tables 1-3 of this section.***

### 9.0 Randomization/Allocation and Participant Assignment

This section of the MOP should describe the method used to prospectively assign participants to the study intervention such as through randomization and treatment allocation for single-arm studies. Randomization and/or participant assignment procedures may include but are not limited to:

* ***Assignment Plan*:** The method used for generating randomization codes or the process used to assign participants to the intervention groups.
* ***Process Responsibilities*:** The individual who maintains the master randomization list must be identified. This person is responsible for assigning randomization codes, notifying appropriate study team that the participant has been randomized, and securely storing all randomization files. If another process besides randomization is used to assign participants to groups, that process should also be described.
* ***Procedure for Randomizing or Assigning a Participant:*** The individual who is responsible for initiating the randomization or assignment procedure must be identified. This individual must know whom to contact once a potential participant is determined eligible for a study, which forms must be completed prior to randomization/assignment (e.g., informed consent form and participant eligibility form), what tool(s) (i.e., web-based) or method(s) will be used and how to use the tool(s).

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

***Sample Text:***

***Before randomizing the participant, you must:***

1. ***Apply inclusion and exclusion criteria to the participant.***
2. ***Obtain signed consent form.***
3. ***Have agreement to randomize from the site investigator.***
4. ***Know your site’s username and password.***
5. ***Have the participant’s exact age.***
6. ***Have a pen ready to record participant ID and intervention allocation.***

***Internet Randomization: The unblinded Study Coordinator will log onto the Internet randomization system through the Internet website (***[***www.randomization.com***](http://www.randomization.com)***) and click on the Randomization button. This will take you directly to the login screen. Enter the login name and password specific to your site in order to access the website. After you have entered your site’s login and password, you will reach the home screen. Select the “Randomize Participant” option from the left-hand side toolbar on the home screen. You will be taken to the Randomization “Step 1” Screen where you will be asked to enter the participant eligibility information. The next step “Step 2” will ask you to verify that the participant information you entered is correct. If it is correct, you can click the “Next” button. If you see a mistake, please click on the “Back” button to correct the mistake. Step 3 is where the person who is randomizing the participant needs to enter their initials. This is not the participant’s initials, but the initials of the individual who is randomizing the participant. Once you have entered your initials, you can click on the “Randomize” button to complete the randomization process. The final screen will show you the intervention group assignment for the participant, including their participant ID number in the study.***

**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 team 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 product 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 study interventional drug in a locked refrigerator in room 305B. It will be stored at 36 degrees Fahrenheit plus/minus 2 degrees, to be checked twice a day by the Research Pharmacist. The Research Pharmacist will check the refrigerator temperature log on Mondays, Wednesdays, and Fridays to ensure that the logs are being completed. In the event the refrigerator temperature was noted to be above 40 degrees Fahrenheit, the Research Pharmacist will contact the drug provider for guidance immediately.***

***The interventional drug should be stored in a refrigerator at all times (when not being administered), to be stored between 34- and 38-degrees Fahrenheit. The study medication should not be exposed to light. Unused or discarded interventional drugs 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 01APR2020) were received from the University Pharmacy Department on 01 May 2020. 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 Masking and Unmasking

This section of the MOP should describe in detail the investigator’s procedures for unmasking.

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

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

***Sample Text:***

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

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

* The identification of the unmasked participant,
* The reason for unmasking,
* The study team members responsible for unmasking, and
* A list of study team members who are not masked.

### 11.0 Study Visit Schedule and Procedures

This section of the MOP should start with an overview of the study visits and schedule and the subsequent subsections should describe all the study visits, the timeline and the process for completing them in step by step detail. All endpoint or outcome evaluations (i.e., improvement in symptoms) and safety evaluations (e.g., blood chemistries) should be identified and explained in detail. The schedule of when evaluations take place must also be specified (i.e., five hours after the last dose of study drug/placebo administration).

#### 11.1 Study Visit Schedule

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 below. Please add the study visit schedule in this section of the MOP and ensure that the visit windows (i.e., +/- 5 days) are clearly defined in both the MOP and the study protocol.

**Sample schedule:**

| **Visit Description**Study Visits/ Study days (or weeks) *{Note: visit windows should be added within this table}* | **Screening**Visit -1Day -14 to Day -1 | **Intervention Phase and Follow-up**Visit 1Day 0/ Randomization | **Intervention Phase and Follow-up**Visit 2Week 2 | **Intervention Phase and Follow-up**Visit 3Week 4 | **Intervention Phase and Follow-up**Visit 4CrossoverWeek 8 | **Intervention Phase and Follow-up**Visit 5Week 10 | **Intervention Phase and Follow-up**Visit 6Week 12 | **Intervention Phase and Follow-up**Visit 7Week 16/End of Study |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Informed Consent | X |  |  |  |  |  |  |  |
| Demographics |  |  |  |  |  |  |  |  |
| Joint Exam |  | X |  |  | X |  |  | X |
| Medical History | X | X | X | X | X | X | X | X |
| Prior Medications | X |  |  |  |  |  |  |  |
| Physical Exam | X |  |  |  |  |  |  | X |
| Blood Pressure | X | X | X | X | X | X | X | X |
| Height | X | X | X | X | X | X | X | X |
| Weight | X | X | X | X | X | X | X | X |
| Muscle Strength Test | X | X | X | X | X | X | X | X |
| Chemistries | X | X |  | X | X | X | X | X |
| Liver and Kidney Function Tests | X | X | X | X | X | X | X | X |
| Hematology | X | X | X | X | X | X | X | X |
| Pregnancy Test | X | X |  |  | X | X | X | X |
| Randomization |  | X |  |  |  |  |  |  |
| Intervention Administration |  | X | X | X | X | X | X |  |
| Concomitant Medications | X | X | X | X | X | X | X | X |
| Adverse Events |  | X | X | X | X | X | X | X |
| Study Completion |  |  |  |  |  |  |  | X |

**Visit Schedule Checklist:**

* **Have you covered each visit and participant contact?**
* **Have you specified when each visit takes place and the visits windows?**
* **Have you confirmed that every procedure is listed in the table?**

#### 11.2 Visit Procedures

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

**Sample Text:**

***Upon notification that participant has arrived at the hospital waiting room, the Study Coordinator must notify the site investigator that the participant is ready. The Study Coordinator should then notify the Pharmacy that the participant for the study is present and arrange the delivery of intervention. Refer to Section 10.0 for masking/unmasking procedures.***

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

***Post-intervention administration, the Study Coordinator will conduct the Numeric Rating Scale (NRS) assessment (see section 16.0 for form specific completion instructions). 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 after the completion of the intervention phase. Additionally, it should also include details about processes and procedures to follow if a participant discontinues the study intervention before study completion.

***Sample Text:***

***Participants will be followed through all study visits through 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 intervention before study completion, every effort will be made by the study team to have the participant continue to complete all other study procedures. However, if the participant is not willing to continue study participation, the study team will attempt to collect the final visit data.***

### 12.0 Concomitant Medications

Please list all allowable and/or excluded concomitant medications in this section of the MOP. In addition, 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.). The form/log should be included as an appendix.

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

* ***Gabapentin***
* ***Aspirin***

### 13.0 Safety Reporting

This section of the MOP must detail the definitions of and procedures for reporting adverse events, serious adverse events, and unanticipated problems. Please follow specific requirements and guidance outlined in the NIAMS Reportable Events Requirements and Guidelines for Investigators Conducting NIAMS-funded Clinical Research Studies (<https://www.niams.nih.gov/grants-funding/conducting-clinical-trials/clinical-trial-policies-guidelines-and-templates/data-1>).This section should follow the OHRP and/or FDA guidelines, whichever is applicable to your study. This section should also include definitions for categorizing severity (e.g., mild, moderate, and severe), relatedness (e.g., not related, possibly/probably related, or definitely related to the study intervention), and expectedness (e.g., expected vs. unexpected) of adverse events and serious adverse events.

Please note that severity and seriousness should not be used interchangeably. Severity refers to a classification of the intensity of an event, whereas seriousness serves as a guide for defining regulatory reporting obligations (e.g. adverse event vs. serious adverse event).

Similarly, unexpected adverse events and unanticipated problems are also often mistaken for each other. An unexpected adverse event is any event that is not included as an expected event in the protocol, informed consent form, or package insert/investigator’s brochure (as applicable for the study). However, an event must meet specific expectedness, relatedness, and safety requirements to be considered an unanticipated problem as defined below. Unanticipated problems may occur that are not considered to be adverse events, as adverse events/serious adverse events are only a small subset of possible unanticipated problems.

#### 13.1. Adverse Event (AE), Serious Adverse Event (SAE), and Unanticipated Problem (UP) Definitions

**Sample Text:**

* ***Adverse Event – Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research.***
* ***Serious Adverse Event – Any adverse event temporally associated with the subject’s participation in research that meets any of the following criteria:***
1. ***results in death;***
2. ***is life-threatening (places the subject at immediate risk of death from the event as it occurred);***
3. ***requires inpatient hospitalization or prolongation of existing hospitalization;***
4. ***results in a persistent or significant disability/incapacity;***
5. ***results in a congenital anomaly/birth defect; or***
6. ***any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).***
* ***Unanticipated Problems – 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.***

#### 13.2 Adverse Event Reporting

In this section of the MOP, the procedure for collecting, assessing and reporting AEs should be detailed, including the role of the study PI, site investigator and study Medical Monitor (if applicable). In addition, a sample AE form/log should be included as an appendix.

Requirements for reporting AEs to the NIAMS, the study’s data and safety monitoring body (e.g., Data and Safety Monitoring Board (DSMB) or SO), FDA (if applicable), and IRB should be described in this section. Please note, the NIAMS requires reporting of all adverse events to the NIAMS and monitoring body. All AEs regardless of expectedness or relatedness are reported in aggregate as part of the routine Data and Safety Monitoring Report to the NIAMS and monitoring body; typically, twice per year. For studies not using a monitoring body, AEs are expected to be reported to the NIAMS in the Research Performance Progress Report (RPPR) on an annual basis.

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

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

**Checklist:**

* **How are study team notified of AEs?**
* **Who is responsible for reporting the AE? How soon?**
* **Who is the responsible person for notifying the PI? Medical Monitor? IRB?**
* **After an AE, 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 monitoring body and the NIAMS through the Executive Secretary should be documented. 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 form should be included as an appendix to the MOP.

All SAEs, unless otherwise specified in the study protocol and approved by the IRB and the NIAMS, require expedited reporting by the study PI or site investigator to the study's safety monitoring bodies and the NIAMS. All SAEs (regardless of expectedness or relatedness) must be reported in an expedited manner to the NIAMS and the monitoring body within 48 hours of the investigator becoming aware of the event. For studies not using a monitoring body, it is still required that SAEs be reported to the NIAMS within 48 hours of the investigator becoming aware of the event.

The expedited initial SAE reports should be submitted to the NIAMS and monitoring body with any available information and it is acceptable if the report is not complete. Follow-up reports should be provided as additional information becomes available. All SAEs must be followed to resolution and a final report submitted detailing the outcome.

Studies using FDA regulated drugs, biologics or devices must follow FDA reporting requirements.

Note: Given that the NIAMS, IRB, and FDA reporting timelines can vary, investigators should adhere to all applicable reporting requirements and outline a process that will be followed for the study.

A sample of the SAE form is shown in **Appendix B**.

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

**SAE Checklist:**

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

#### 13.4 Unanticipated Problems Reporting

This section of the MOP should describe the procedures for reporting unanticipated problems to the NIAMS, monitoring body, FDA (if applicable), OHRP, and IRB. Please note that per the NIAMS reporting requirements, unanticipated problems must be reported to the NIAMS and the monitoring body within 48 hours of the investigator becoming aware of the event. The initial UP report is acceptable even if the report is not complete. Follow-up reports should be provided as additional information becomes available. For studies not using a monitoring body, it is still required that UPs be reported to the NIAMS within 48 hours of the investigator becoming aware of the event. OHRP provides guidance for reporting unanticipated problems to the IRB at Unanticipated Problems Involving Risks & Adverse Events Guidance (2007) (<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems#Q5>).

A sample UP form is shown in **Appendix C.**

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

**Checklist:**

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

### 14.0 Data and Safety Monitoring Activities

The roles and responsibilities of the entities monitoring participant safety and data quality should be briefly described in this section with the full details included in a separate Data and Safety Monitoring Plan (DSMP). To ensure proper monitoring, the NIAMS has made available a template and guidelines for how to write a DSMP. Please reference the DSMP in this section. The template and guidance document can be found at How to Write a Data and Safety Monitoring Plan (<https://www.niams.nih.gov/grants-funding/conducting-clinical-research/clinical-trial-policies-guidelines-and-templates/data>).

### 15.0 Study Compliance

This section of the MOP should describe relevant protocol deviations and the reporting process to appropriate parties, including the study PI or site investigator, the NIAMS, the monitoring body, and the IRB. The study should adhere to the IRB policies for reporting protocol deviations. In addition, the reporting of deviations should be discussed with the NIAMS and the monitoring body prior to study start and be clearly outlined in the data and safety monitoring plan.

Per the NIAMS reporting requirement, any protocol deviations that impact participant safety must be reported to the NIAMS and the monitoring body within 48 hours of the investigator becoming aware of the event. All other protocol deviations that do not impact participant safety are reported in aggregate as part of Data and Safety Monitoring Report to the NIAMS and monitoring body. For studies not using a monitoring body, investigators should follow their Institution’s policies for reporting to the IRB. This section should also describe the mitigation measures that will be taken by the site investigator should protocol deviations occur to ensure no further issues.

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

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

The study site should maintain a log of all protocol deviations and should report them as specified in the DSMP to the NIAMS and the monitoring body. A sample log is presented in **Appendix D** and should be included as an appendix to the MOP.

### 16.0 Data Collection and Study Forms

This section of the MOP should describe the study’s data collection. Copies of all forms should be included as an appendix. Study forms, also called case report forms (CRFs), provide the vehicle for consistent data collection. Sample CRFs for demographics, medical history, prior and concomitant medications, vital signs, and study disposition are shown in **Appendices G-1** through **G-5**.

**Sample Text:**

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

***Knee injury and Osteoarthritis Outcome Score (KOOS)***

***The KOOS consists of 42 items in 5 domains that separately measure pain, other symptoms, function in daily living, function during sports/recreation and knee-related Quality of Life (QOL). Domain scores represent the sum of all items in the domain standardized to a score from 0 to 100 (worst to best).***

***If a mark is placed outside of a box, the box closest to the box is chosen. If two boxes are marked, the box that which indicates the more severe problem is chosen. If at least 50% of the subscale items are answered for each subscale, a mean score can be calculated. If more than 50% of the subscale items are omitted, the response is considered invalid and no subscale score should be calculated. For KOOS Pain, this means that 5 items must be answered; for KOOS Symptoms, 4 items; for KOOS ADL, 9 items; for KOOS Sport/Rec, 3 items; and for KOOS QOL, 2 items must be answered to calculate a subscale score. Subscale scores are independent and can be reported for any number of the individual subscales, i.e. if a particular subscale is not considered valid (for example, KOOS Sport/Rec 6 weeks after ACL reconstruction), the results of the other subscales can be reported at that time-point. Scores will be calculated automatically by the Data Management System.***

***The KOOS will be administered at the screening/baseline visit before surgery and at 6 weeks, 3, 6, 12 and 24 months post-operatively by direct participant entry into the Data Management System or by using the CRF template accessible in the file repository and entered by the Study Coordinator.***

**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 study team member for updating/editing/approving**
* **Maintenance of forms**
* **Participant binder setup**
	+ **Include responsible study team member**

#### 16.1 Source Documentation

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

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

***Sample Text:***

***Physical Examination form, signed by participant’s physician***

***Received within 30 days after enrollment from participant before receiving intervention, signed and dated. The site investigator may contact participant’s physician with any concerns.***

***The site investigator 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., laboratory reports, ECG tracings, x-rays, radiology reports, etc.)**
* **Signed consent forms**
* **CRFs**
* **Data correction forms**
* **Workbooks**
* **Questionnaires completed by the participant**

#### 16.2 General Instructions for Completing Forms

In this section of the MOP, if CRFs are used in the study, please provide a set of instructions for completing CRFs to ensure quality and consistency in data collection. Some useful and frequently used examples are listed below. These instructions should be in accordance with section 4.9 of the guideline for GCP ICH E6 (R2): <https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf>.

***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, laboratory 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.***

#### 16.3 Retention of Study Documentation

The length of time all study files are to be maintained should be specified in this section. In general, federal regulation requires that studies supported by a federal government grant retain participant forms for three years, while studies conducted under a federal contract must retain participant forms for seven years. Please pay special attention to studies involving children, as study documentation retention procedures are often longer in duration and more comprehensive. Details about the federal policies surrounding record retention and access can be found at [2 CFR Part 215](https://www.whitehouse.gov/sites/whitehouse.gov/files/omb/circulars/A110/2cfr215-0.pdf). The FDA, IRBs, institutions, sponsors, states, and countries may have different requirements for record retention; investigators should adhere to the most rigorous requirements and should retain forms and all other study documents for the longest applicable period. This specific period should be stated in the MOP.

**Sample Text:**

***After the study ends, the study team shall maintain participant forms in a secure location for three years, as indicated by the protocol, federal regulations, and IRB guidance.***

**Checklist:**

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

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

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

#### 16.4 Administrative Forms

In this section of the 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.

### 17.0 Data Management

This section of the MOP should describe the data management approach and computer system, if applicable, that will support the study. It should detail how data are to be entered (either direct at time of data collection or recorded first on paper source and entered into an Electronic Data Capture system at a later time), and/or edited.

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

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

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

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

**Sample Text:**

***The BON system, or Binary Online Network, is a data entry system that captures simple participant vital signs utilizing a keyboard number pad only. Any study team member can enter this using the BON iPhone App while standing next to a participant’s 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 participants can be sent to departmental email through the app.***

#### 17.1 External Data

External data refers to data sent to or collected at a laboratory or imaging facility (e.g., blood samples, MRIs, etc.). This section of the 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 HIPAA guidelines, personal identifiers such as name, geographic location, social security number, and fifteen other specific individual identifiers should not be used (see page 21 above). Therefore, it is important to specify how participant materials will be identified (e.g., by participant identification number) during transmission.

***Sample Text:***

* ***X-Ray of Spine***
	+ ***Collected by Radiology at Hospital Center on Participant’s Initial Visit***
		- ***2 Standard Images are transferred via departmental envelope to physician by Hospital Administrative study team member***
		- ***Images are de-identified by Radiology***
		- ***Images are labeled with Study ID by Study Coordinator at arrival to site investigator’s office***
		- ***Images are kept in a separate locked cabinet in research office***

**External Data Checklist:**

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

#### 17.2 Quality Control Procedures

This section should detail the various aspects of the QC plan for the study and describe any training and certification procedures. It may include SOPs, data and form checks, monitoring, routine reports, and correction procedures.

##### 17.2.1 Standard Operating Procedures

SOPs which relate to the conduct of the clinical trial 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 the study team.

##### 17.2.2 Data and Form Checks

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

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

##### 17.2.3 Clinical Site Monitoring

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

Please add any site monitoring or audit visit activities, plans to review data quality in the study database and source documentation, as well as plans to verify adherence to the study protocol and GCP. Each site’s plan for monitoring, including a monitoring timeline, should be described.

Site monitoring may be conducted through periodic site visits (either in person or remote) during the study. The frequency of visits may depend upon the site's performance and the number of participants enrolled. If no site visits are planned, it should be noted in this section along with the rationale.

### 18.0 Reports

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

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

***Sample Text:***

* ***Monthly Status Update***
	+ ***Delivered to the NIAMS through the Executive Secretary until the first participant is enrolled***
	+ ***Produced by the Study Coordinator***
* ***Monthly Enrollment Report***
	+ ***Delivered to the DSMB and the NIAMS through the Executive Secretary by the 5th of each month after 1st participant is enrolled***
	+ ***Produced by the Study Coordinator***

### 19.0 Study Completion and Closeout Procedures

Study closeout activities are to be performed once the study reaches completion or if the study is terminated early for any reason. The closeout activities are performed to confirm that the 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 Closeout procedures. Details should be included in the subsequent sections.

***Examples of Closeout activities include, but are not limited to, the following:***

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

Additional closeout activities can be found in **Appendix H**.

#### 19.1 Participant Notification

In this section of the MOP, please include each site’s plan to notify participants when the study is complete. The study PI and study team should develop a plan in coordination with each site to notify participants that the study is over, ask whether they would like to be informed of the results, and thank them for their participation. It may include either the first article or a reference to the article.

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

### 20.0 Policies

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

#### 20.1 Confidentiality Procedures

This section of the MOP will discuss the safeguards that have been put in place by the study PI to ensure participant confidentiality and data security. It is the responsibility of the study PI and site investigator(s) to outline and enforce participant confidentiality and data security guidelines. 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 forms.
* ***Data listings*** *-*participant name, name code, hospital chart, record number, Social Security Number, or other unique identifiers should not be included in any published data listing.
* ***Data distribution*** - data listings that contain participant name, name code, or other identifiers easily associated with a specific participant should not be distributed.
* ***Data disposal*** - computer listings that contain participant-identifying information should be disposed of in an appropriate manner.
* ***Access*** - participant records should not be accessible to persons outside the study site without the express written consent of the participant.
* ***Storage*** *-*study forms and related documents retained both during and after study completion should be stored in a secure location. If computers are used to store and/or analyze clinical data, the investigator should address the following elements of computer security to ensure that the data remain confidential.
* ***Passwords*** - Passwords provide limitations on general access to computer systems and to the functions that individuals can use. Passwords should be changed on a regular basis.
* ***User training*** -Study team members with access to clinical computer systems should be trained in there 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 (e.g. 50%) so that backup tapes are not damaged.

#### 20.2 Publications

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

Any plans to publish study results prior to study completion should be reviewed by the NIAMS and the study’s data and safety monitoring body to ensure study integrity is maintained.

This section should include a publication and data sharing policy statement and instructions for the mandatory submission of the final, peer-reviewed manuscripts to the NIH National Library of Medicine’s PubMed Central for archiving upon acceptance for publication. Please refer to the policy details at NOT-OD-08-033: Revised Policy on Enhancing Public Access to Archived Publications Resulting from NIH-Funded Research (<https://grants.nih.gov/grants/guide/notice-files/not-od-08-033.html>).

Additionally, investigators conducting clinical trials funded in whole or in part by the NIH are expected to ensure that the trial results are submitted to ClinicalTrials.gov. The Final Rule for Clinical Trials Registration and Results Information Submission ([42 CFR Part 11](https://www.ecfr.gov/cgi-bin/text-idx?SID=e617ec4da22678f934787ed565bbaa5a&mc=true&node=pt42.1.11&rgn=div5)) clarifies and expands the regulatory requirements and procedures for submitting registration and results information for certain trials to ClinicalTrials.gov, in accordance with FDAAA 801.

### 21.0 MOP Maintenance

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

The footer on each page of the MOP should include the study 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 study team to ensure 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. This should be the first page of the MOP.

## 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 team to learn the details of the study and to develop precise procedures that are understood and followed during the study.