# How to Write a Data and Safety Monitoring Plan (DSMP)

December 2020

# PREFACE

*Investigators should consider using this template when developing the Data and Safety Monitoring Plan (DSMP) for clinical studies supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS).*

*The goal of the DSMP is to provide a general description of a plan that you intend to implement for data and safety monitoring. The DSMP should specify the following:*

* *A brief description of the study design*
	+ *Primary and secondary outcome measures/endpoints*
	+ *Sample size and target population*
	+ *Inclusion and exclusion criteria*
	+ *A list of proposed participating sites and centers for multi-site trials*
* *Potential risks and benefits for participating in the study*
* *Procedures for data review and reportable events*
* *Roles and responsibilities of study staff and monitoring entity (referred to as “Monitoring Body”). These can include, but are not limited to, monitoring by a:*
	+ *Project Director (PD)/Principal Investigator (PI) (required)*
	+ *Institutional Review Board (IRB) (required)*
	+ *Designated medical monitor*
	+ *Internal Committee or Board*
	+ *Independent, NIAMS-appointed Monitoring Body (MB) which can include a Data and Safety Monitoring Board (DSMB), an Observational Study Monitoring Board (OSMB), a Safety Officer (SO) or Dual SOs*
* *Content and format of the safety report*
* *Data Management, Quality Control and Quality Assurance*

*Note that all instructions and sample text are shown in blue italics and should be replaced with the study specific text. There is no need to include sections that are not relevant to the particular study.* **Please do not use the sample text verbatim.**

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# 1.0 STUDY OVERVIEW

## 1.1 Study Description

*{This section outlines the overall goal of this project. It also describes the study design, primary and secondary outcome measures/endpoints, sample size/power calculation and target population, inclusion and exclusion criteria.}*

## 1.2 Study Management

{This section includes the proposed participating sites and their responsibilities. In addition, this section should include the planned enrollment timetable (i.e. projected enrollment).}

# 2.0 Participant Safety

## 2.1 Potential Risks and Benefits for Participants

{This section outlines the potential risks and benefits of the research for the study participants and for society. It should include a description of all expected adverse events (AEs), the known side effects of the intervention, and all known risks or complications of the outcomes being assessed.}

### 2.1.1 Potential Risks

{Outline potential risks for study participants including a breach of confidentiality.}

{Begin sample text}

The potential risks to study participants include but are not limited to temporary slight discoloration of the skin after blood draws and pain at the blood draw site.

{End sample text}

### 2.1.2 Potential Benefits

{Outline potential benefits for study participants or if there are no direct benefits to the participants.}

{Begin sample text}

The potential benefits to study participants include but are not limited to ongoing nutritional counseling will be provided to all participants.

{End sample text}

## 2.2 Protection Against Study Risks

{This section provides information on how risks to participants will be managed. It should specify any events that would preclude a participant from continuing in the study. In general, the format and content of this section are similar to the Human Participants section of the grant application.

In addition, this section describes measures to protect participants against study specific risks including the data security to protect the confidentiality of the data.}

{Begin sample text}

The procedures to protect against risks *(describe known risks)* include *(e.g., a safe, hygienic environment for all medical procedures and an experienced, certified staff.)*

{End sample text}

### 2.2.1 Informed Consent Process

{This section explains the informed consent process. It should include, but not be limited to, who will be consenting the participant, how and under what conditions will a participant be consented, and that participation is voluntary. The informed consent process should meet the revised Common Rule requirements for consenting. For further details on this requirement, please visit: <https://www.ecfr.gov/cgi-bin/text-idx?SID=921afb2e7909a2cf08c5f3ce160a0c96&mc=true&node=se45.1.46_1116>}

{Begin sample text}

Before individuals may participate in any screening procedures, informed consent will be obtained. The study team intends to follow guidelines to ensure that all participants consent obtained will be as informed and voluntary as possible. The potential participant will be informed that participation is voluntary, and he/she has the right to stop at any time. In addition, the informed consent process will meet the revised Common Rule requirements for consenting. These include but are not restricted to:

1. Study Information – Participants should be fully informed about the study by appropriately trained study staff and have adequate time to evaluate the pros and cons of participation.
2. Study Discussion – Participants should be encouraged to discuss the study with anyone they wish, particularly family and friends who might be affected (for example, persons who might be needed to provide transportation).
3. Study Data Security – Participant will be informed that study data will be de-identified to protect participant privacy and against possible identifiability.
4. Biospecimen collection – Participants will be given the option to provide open-ended consent for most research uses of a variety of biospecimens collected. Each sample will be stripped of identifiers.
5. No Proxy Consent – To be eligible for participation in the study, participants must have the capacity to give their own informed consent.
6. Environment for Informed Consent – The setting in which consent is obtained should be as private as possible so participants can freely ask questions without embarrassment.
7. Obligations – The participant should be given a copy of the informed consent forms after they are signed, dated and witnessed.
8. Copies of Informed Consent – Participants will be encouraged to keep the consent forms.
9. Witness Signature and Source Documentation – Anyone who signs a consent form will be asked to personally date it.

***{End sample text}***

# 3.0 REPORTABLE EVENTS

## 3.1 Definitions

{This section should describe how to identify AEs, SAEs and UPs. In the case where the intervention is a Food and Drug Administration (FDA) regulated drug, device or biologic, it should include the FDA definition, grading scale and “study relatedness” criteria of AEs.}

### 3.1.1Adverse Events (AEs)

{The definition of adverse event here is drawn from the OHRP guidance (<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html>); for some studies, the ICH E6 definition may be more appropriate. Expected and unexpected AEs should be listed in this section.}

{Begin sample text}

An AE is defined as 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.

For the purposes of this study, AEs include any new events not present during the pre-intervention period or events that were present during the pre-intervention period which increased in severity. Examples of AEs include but are not limited to the following:

* A clinically significant laboratory or clinical test result
* An event that occurs as a result of a study procedure

{End sample text}

### 3.1.2Serious Adverse Events (SAEs)

{SAEs are a subset of all AEs.}

{Begin sample text}

SAEs are defined as any adverse event temporally associated with subject’s participation in research that meets any of the following criteria:

* Results in death
* Is life-threatening (places the subject at immediate risk of death from the event as it occurred)
* Requires inpatient hospitalization or prolongation of existing hospitalization
* Results in a persistent or significant disability/incapacity
* Results in congenital anomaly/birth defect
* Any other adverse events 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)

{End sample text}

### 3.1.3 Unanticipated Problems (UPs)

{The OHRP definition of UPs can be accessed using the link provided in Section 3.1.1 above.}

{Begin sample text}

UPs can be either AE/SAEs, which are unexpected events that relate directly to participant safety, or protocol deviations that put patient privacy at risk or put patients at risk in some way that does not have an impact on their health and safety.

Unanticipated problems are defined as any incident, experience, or outcome that meets **all** of the following criteria:

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

SAEs that are unexpected and related or possibly related to participation in research are considered to be UPs because such events always suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized.

{End sample text}

### 3.1.4 Protocol Deviations

{This section should include the study definition of protocol deviations and define the events placing the participant at increased risk of harm or compromising the integrity of the safety data.}

{Begin sample text}

A protocol deviation is generally an unplanned excursion from the protocol that is not implemented or intended as a systematic change.

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

* Enrollment or randomization of an ineligible participant
* Failure to obtain informed consent
* Wrong intervention administered to participant
* Unreported SAEs
* Improper breaking of the blind
* Use of prohibited medication
* Mishandled samples
* Multiple visits missed or outside study windows

{End sample text}

## 3.2 Collection and Assessment of AEs, SAEs, UPs, and Protocol Deviations

*{The section should include who is responsible for collecting these events, how the information will be captured, where the information will be collected from (e.g., medical records, self-reported), and what study form(s) will be used to collect the information (e.g., case report forms, direct data entry). This section should also include what type of information will be collected (e.g., event description, time of onset, assessment of seriousness, relationship to the study intervention, severity, etc.). Note that it is the NIAMS requirement to collect all AEs regardless of the expectedness or relatedness.*

*This section should also describe who is responsible for assessing these events. The individual(s) responsible should have the relevant clinical expertise to make such an assessment (e.g., physician, nurse practitioner, physician assistant, nurse). When assessing AEs and SAEs, the following information should be included:*

* *Relationship to study intervention*
	+ - *Related*
			* *Possibly/Probably (may be related to the intervention)*
			* *Definitely (clearly related to the intervention)*
		- *Not Related (clearly not related to the intervention)*
* *Expectedness*
	+ *Expected*
	+ *Unexpected*
	+ *Severity (Describe the method of grading an adverse event for severity. Please note that a severe AE and an SAE are distinct terms)*
		- *Mild*
		- *Moderate*
		- *Severe}*

{Begin sample text}

All AEs will be collected from the date the informed consent form is signed until the final study visit. For events that occur between visits, participants are queried on a routine basis about every two weeks post-randomization through their final study visit.

AEs will be captured on the appropriate case report form. Information to be collected includes event description; time of onset; assessment of seriousness, severity, relationship to study procedures or interventions, and expectedness; medical care received; outcome of event; and time of resolution/stabilization of the event.

All AEs occurring while on study are documented appropriately regardless of relationship. All AEs/SAEs will be followed until satisfactory resolution or the participant is stable.

All AEs will be assessed by the investigator for severity, expectedness, and relationship to the intervention using the protocol-specified definitions.

{End sample text}

## 3.3 Reporting of AEs, SAEs, UPs, Protocol Deviations, Serious or Continuing Noncompliance, and Suspension or Termination of IRB Approval

*{This section should describe who is responsible for reporting these events and the roles and responsibilities of each person on the clinical study team who is involved in the safety reporting to the IRB, FDA (if applicable), Monitoring Body, and NIAMS (through the NIAMS Executive Secretary). It should also include the* [*Office for Human Research Protections (OHRP)*](https://www.hhs.gov/ohrp/compliance-and-reporting/guidance-on-reporting-incident/index.html) *and* [*FDA*](https://www.fda.gov/drugs/investigational-new-drug-ind-application/ind-application-reporting-safety-reports) *reporting requirements. See* [*NIAMS Reportable Events Requirements and Guidelines*](https://www.niams.nih.gov/grants-funding/conducting-clinical-trials/clinical-trial-policies-guidelines-and-templates/data-1) *for more details.*

*The NIAMS SAE Report Form template can be accessed here: XX}*

### 3.3.1 AE Reporting Procedures

*{All non-serious AEs (regardless of expectedness or relatedness) are reported to the Monitoring Body and NIAMS (through the NIAMS Executive Secretary) semi-annually or as determined by the NIAMS.}*

{Begin sample text}

All AEs are reported in aggregate as part of the routine data and safety monitoring report provided to the Monitoring Body and NIAMS (through the NIAMS Executive Secretary). AEs are reported to the IRB as part of the continuing review.

{End sample text}

### 3.3.2 SAE Reporting Procedures

*{All SAEs (regardless of expectedness or relatedness) must be reported in an expedited manner to the NIAMS and the Monitoring Body. There may be different timeline for reporting SAE to the IRBs, FDA (if applicable), Monitoring Body and the NIAMS. The timeline for reporting SAEs to the Monitoring Body and NIAMS (through the NIAMS Executive Secretary) is* ***within 48 hours of the investigator becoming aware of the event****so that a real time assessment can be conducted, and the outcome shared in a timely manner.}*

***{Begin sample text}***

All SAEs (regardless of expectedness or relatedness) will be reported to the Monitoring Body and NIAMS (through the NIAMS Executive Secretary) within 48-hours of the investigator becoming aware of the event. The study team will utilize the study specific SAE report form to collect the information and the investigator will conduct and provide an assessment of each event. Other relevant medical information will be completed on all SAEs regardless of expectedness or relatedness. This data will be entered in the study electronic database capture system.

The expedited initial SAE reports should be submitted 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.

{End sample text}

### 3.3.3 UP Reporting Procedures

*{All events that meet the criteria of a UP must be reported in an expedited manner to the NIAMS and the Monitoring Body. There may be different timeline for reporting UPs to the IRBs, OHRP/FDA (if applicable), Monitoring Body, and the NIAMS. The timeline for reporting UPs to the Monitoring Body and NIAMS (through the NIAMS Executive Secretary) is* ***within 48 hours of the investigator becoming aware of the event*** *so that a real time assessment can be conducted, and the outcome shared in a timely manner.}*

{Begin sample text}

If UPs occur during the study, they will be reported to the IRB, Monitoring Body, and NIAMS by the study team*.* The UP report for the Monitoring Body and NIAMS will be completed and submitted to the NIAMS Executive Secretary **within 48 hours of the investigator becoming aware of the event**.

All events that meet the requirements of a UP are reported to the IRB in accordance to their policy, within 10 days of participant disclosure to a clinical site.

{End sample text}

### 3.3.4 Protocol Deviation Reporting Procedures

{Protocol deviations impacting participant safety are subject to expedited reporting to the Monitoring Body and NIAMS (through the NIAMS Executive Secretary) **within 48 hours of the investigator becoming aware of the event** so that a real time assessment can be conducted, and the outcome shared in a timely manner**.** All other events should be reported at the time of the routine DSMB meeting or submission of the safety report.}

{Begin sample text}

Protocol deviations that may impact participant safety will be reported to the Monitoring Body and NIAMS (through the NIAMS Executive Secretary) within 48 hours of the investigator becoming aware of the event. These may include, but are not limited to, the following:

* Inclusion/exclusion criteria not met
* Unreported SAEs
* Use of prohibited medication
* Incorrect lab tests drawn or missing lab tests
* Intentional deviation from protocol, Good Clinical Practice, or regulations by study personnel

Protocol deviations that do not impact participant safety will be reported in aggregate as part of the routine data and safety monitoring report sent to the Monitoring Body and NIAMS.

Protocol deviations are reported to the IRB in accordance to their policy, within 10 days of identification of the event.

{End sample text}

### 3.3.5 Serious or Continuing Noncompliance

*{This section should include the process in place at your institution to capture and report serious or continuing noncompliance. It should include who is responsible for reporting. Serious or continuing noncompliance must be reported to the NIAMS Program Officer and Grants Management Specialist within 3 business days of IRB determination. A copy of the IRB submission and determination must be submitted along with the report to the NIAMS. The guidance on reporting incidents to OHRP should also be followed to provide the timeline of reporting to this regulatory body.}*

{Begin sample text}

The study team plans to comply with research regulations and institutional policies and procedures to minimize risk to participant safety and increase adherence to the study protocol. However, if for any reason the study fails to follow the applicable laws, policies, regulations, or the provisions of the IRB-approved research study, it will report the event as a noncompliance (serious or continuing) to all the oversight bodies, including but not limited to the IRB, NIAMS, and OHRP. Per institutional policy, the investigator will report the event to the IRB within 48 hours of becoming aware of the noncompliance. If the IRB makes a determination that the event is a result of noncompliance (either serious or continuing), it will be reported to the NIAMS Program Officer and Grants Management Specialist within 3 business days of IRB determination. A copy of the IRB submission and determination will be submitted along with the report. The OHRP will also be notified within 3 business days of IRB determination.

***{End sample text}***

### 3.3.6 Suspension or Termination of IRB Approval

{This section should include the process for reporting study suspension or termination by the IRB. It should also include who is responsible for reporting to the NIAMS, OHRP, and the timeline for reporting of these events. Suspension or termination of IRB approval must include a statement of the reason(s) for the action and must be reported promptly to the NIAMS Program Officer and Grants Management Specialist within 3 business days of receipt by the PI.}

{Begin sample text}

If the IRB suspends or terminates the study, the investigator will adhere to requirements for reporting to all oversight bodies, including but not limited to the NIAMS and OHRP. Suspension or termination of approval will include a statement of the reason(s) for the action and will be reported to the NIAMS Program Officer and Grants Management Specialist within 3 business days of receipt by the PI. The OHRP will also be notified, at the same, within 3 business days of receipt by the PI.

{End sample text}

# 4.0 INTERIM Analysis & stopping rules

{This section provides information on planned interim analysis. Interim analysis may be conducted either due to pre-specified stopping rules as outlined in the protocol and at predetermined intervals, or as determined necessary by the Monitoring Body to assess safety concerns or study futility based upon accumulating data. An interim analysis may be performed for safety, efficacy and/or futility, and the reports are prepared by the unmasked study statistician or data coordinating center responsible for generating such reports. Rules for stopping the study, based on interim analysis, should be described.

If no interim analysis is planned, this should be noted within this section.}

{Begin sample text}

Interim analysis of the study is planned according to the alpha spending rule [Lan and DeMets, 1994]. The proportion of expected events is considered as the information statistic. The p-values are constructed to maintain the overall study power of 0.05, two-sided. If the test statistic exceeds the boundary, then the study could be considered for early termination due to emerging differences. The interim look is recommended at the end of year one as we expect approximately 50% of the participants followed for at least six months.

{End sample text}

# 5.0 Data and Safety monitoring

{This section identifies the name of the individual or entity responsible for data and safety monitoring, what information will be reviewed, and frequency of such reviews. A brief general introduction regarding data and safety monitoring oversight should be provided in section 5.0, and further details should be provided in the subsequent sections.

***{Begin sample text}***

The investigator will be responsible for ensuring participants’ safety on a daily basis and for reporting Serious Adverse Events and Unanticipated Problems to his or her Institutional Review Board, and the NIAMS and the Monitoring Body (through the NIAMS Executive Secretary), and FDA as required. The Monitoring Body will act in an advisory capacity to the NIAMS to monitor participant safety, evaluate the progress of the study, to review procedures for maintaining the confidentiality of data, the quality of data collection, management, and analyses.

{End sample text}

## 5.1 Frequency of Data and Safety Monitoring

{This section describes the frequency of data and safety monitoring reviews. As the reviews of reportable events (AEs, SAEs, UPs, and protocol deviations) are included in Section 3, this section should focus on the routine and ad hoc review of the full data and safety monitoring reports.}

{Begin sample text}

Data and safety monitoring reports are sent to the Monitoring Body and the NIAMS (through the NIAMS Executive Secretary) in advance of the semi-annual meetings and will include a detailed analysis of study progress, data and safety issues.

Specific triggers for an ad-hoc review or initiation of the process of an ad hoc review will occur if there are unforeseen deaths or the threshold for SAE has been met.

{End sample text}

## 5.2 Content of Data and Safety Monitoring Report

{This section describes the content of the data and safety monitoring reports. The specifics of the study and the requests of the Monitoring Body will guide requirements for additional tables and listings. Tables for multi-site studies will present aggregated data as well as data by site.

For studies with more than one intervention group, this section should indicate the plans for providing data stratified by masked intervention group (i.e., Group A vs. Group B) as part of the closed report to the Monitoring Body, while the open report should have data presented in aggregate without stratification by groups.

The complete data and safety monitoring report template should be included as an appendix.

Refer to the NIAMS Data and Safety Monitoring Board Report Templates ([**https://www.niams.nih.gov/grants-funding/conducting-clinical-research/trial-policies-guidelines-templates/data-safety-monitoring-guidelines-policies/clinical-study-templates-forms**](https://www.niams.nih.gov/grants-funding/conducting-clinical-research/trial-policies-guidelines-templates/data-safety-monitoring-guidelines-policies/clinical-study-templates-forms)) for guidance.}

{Begin sample text}

The study statistician prepares reports that list adverse events, serious adverse events, deaths, and disease-or intervention-specific events required for Monitoring Body review in order to ensure good clinical care and identify any emerging trends. Demographic data will include sex, ethnicity, race, education, and age, and will be stratified by site.

*The data and safety monitoring reports include the following information:*

* *CONSORT diagram and actual versus expected enrollment figures that illustrate recruitment and participation status.[[1]](#footnote-2)*
* *Data tables that summarize demographic and baseline clinical characteristics*
* *Data quality tables that capture missing visits and missing case report forms*
* *Safety assessments of aggregate tables of adverse events and serious adverse events*
* *Listings of adverse events, serious adverse events, deaths, unanticipated problems and protocol deviations*
* *Aggregate tables of clinical laboratory values*

{End sample text}

## 5.3 Monitoring Body Membership and Affiliation

{This section includes a roster of the Monitoring Body’s name(s) and affiliation(s). For studies with a NIAMS-appointed Monitoring Body, the NIAMS Executive Secretary will provide the name(s) and affiliation(s) of the individual(s) serving once the Monitoring Body has been assembled. However, if this is an Internally-appointed Monitoring Body (i.e., PI-appointed), the study team should enter the information in this section once the NIAMS has confirmed that no conflicts of interest with the Monitoring Body member(s) are identified.}

{Begin sample text}

The following individuals have accepted positions as part of the NIAMS-appointed DSMB.

Name
Title, Organization
Area of Expertise

Name
Title, Organization
Area of Expertise

***{End sample text}***

## 5.4 Conflict of Interest for Monitoring Bodies

{This section describes the conflict of interest procedure for Monitoring Body members. For studies with a NIAMS-appointed Monitoring Body, the NIAMS Executive Secretary will conduct a conflict of interest check on each member prior to beginning their service and on an annual basis thereafter. For studies with an Internally-appointed Monitoring Body (i.e., PI-appointed), the study team should provide the name, affiliation, and curriculum vitae (if available) of the proposed Monitoring Body member(s) to the NIAMS Executive Secretary for a conflict of interest check to be conducted. Once the conflict of interest check is complete, this section should be updated to indicate that the NIAMS did not identify any conflicts of interest for the Monitoring Body member(s).}

***{Begin sample text}***

Monitoring body membersshould have no direct involvement with the study investigators or intervention. Each member will sign a Conflict of Interest Statement which includes current affiliations, if any, with any steering committees or advisory councils associated with the study, pharmaceutical and biotechnology companies (e.g., stockholder, consultant), and any other relationship that could be perceived as a conflict of interest related to the study and/or associated with commercial or non-commercial interests pertinent to study objectives.

{End sample text}

## 5.5 Protection of Confidentiality

{This section describes how confidentiality of data presented to the Monitoring Body will be protected.}

{Begin sample text}

Only masked data will be presented during the open sessions of the Monitoring Body meetings. All data, whether in a report or discussed during a MB meeting, are confidential. Participant identities will be kept confidential unless safety concerns necessitate unmasking some or all data.

{End sample text}

## 5.6 Monitoring Body Responsibilities

{A charter provides a detailed list of the Monitoring Body’s responsibilities. Listed in the sample text below are the responsibilities for a NIAMS-appointed Monitoring Body. Please ensure that all of the items are applicable for this study. For studies with an Internally-appointed Monitoring Body, the study team should ensure that a detailed list of the Monitoring Body’s responsibilities are provided in this section.}

{Begin sample text}

The following are the responsibilities of the NIAMS-appointed DSMB:

* Review the research protocol, Data and Safety Monitoring Plan (DSMP), and informed consent documents, including all proposed revisions. The Manual of Operating Procedures (MOP), which may contain the sections included above, is also reviewed
* Evaluate the progress of the study on an ongoing basis, as needed, including periodic assessments of data quality, participant recruitment, accrual and retention, participant risk versus benefit, performance of study site(s), and other factors that can affect the outcome
* Evaluate safety throughout the course of the study through the routine review of aggregated adverse event safety data, in addition to expedited review of unanticipated problems, serious adverse event reports, and protocol deviations impacting participant safety. The DSMB Safety Officer reviews the documentation provided by the study team and makes recommendations to the NIAMS regarding protection of the study participants
* Evaluate proposals of new sites (that differ from the approved application) and make a recommendation to the NIAMS as to whether the enrollment at the site(s) is expected to enhance overall enrollment. Activities include evaluating the patient population pool, catchment area description, recruitment plan, and target enrollment for any new clinical sites
* Consider the impact of factors external to the study when new information, such as scientific or therapeutic developments, becomes available and may affect safety of participants, their willingness to participate in the study or the ethics and conduct of the study
* Assist the NIAMS by commenting on any problems with study conduct or performance
* Ensure that the plan for maintaining the confidentiality of the study data and the results by the investigative team is appropriate
* Review and evaluate requests for protocol modifications
* Review data after completion of each cohort to approve does escalation, if applicable
* Review in advance of the study initiation the study specific stopping rules and plans for interim analyses as established by the PI and selected members of the study team. These plans outline the conditions under which a study may be stopped (e.g., difficulties in recruitment, retention, obtaining outcome measures, or other issues)
* Review the interim analyses and/or accumulating data at the specified interval(s), and as appropriate and make a recommendation to continue, terminate, or modify the study based on observed benefit or harm in accordance with the planned stopping rules

{End sample text}

# 6.0 DATA MANAGEMENT, QUALITY CONTROL, AND QUALITY ASSURANCE

{This section describes how the site will collect, document, and review the data. Who will be responsible for data entry and ensure they are accurate and complete? Which database will be used? Does it have audit tracking capabilities? What is the data query process and frequencies? Are there any planned mitigation strategies in the event of non-compliance? What is the process for locking the final study datasets? Are there any procedures on data access and sharing as appropriate? Is there a description of security measures in place? (If you have a separate Clinical Monitoring and Data Management Plan, please reference it and utilize that information to help populate this section.)

Each study should have standard operating procedures (SOPs) and/or a quality management plan that describe the following (if this is a multi-site study, each site should have SOPs and a plan):

* *Staff training methods and how such training will be tracked*
* *How data will be evaluated for compliance with the protocol and for accuracy in relation to source documents*
* *The documents to be reviewed (e.g., case report forms, clinic notes, product accountability records, specimen tracking logs, questionnaires), who is responsible, and the frequency for reviews*
* *Who will be responsible for addressing quality assurance (QA) issues (correcting procedures that are not in compliance with protocol) and quality control issues (correcting data entry errors). It is anticipated that QA review and data verification will be performed by someone other than the individual originally collecting the data, or by double-data entry. The frequency of internal QA review and measures to be taken for corrective action (e.g., for trends in errors) should be included*
* *QA measures for participant recruitment, enrollment, enrollment targets, and for the validity and integrity of the data****.*** [***E6 Good Clinical Practice (R1): 1.46***](https://www.fda.gov/media/93884/download) *defines quality assurance as “All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with Good Clinical Practice (GCP) and the applicable regulatory requirement(s)”}*
1. Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomized trials. [Ann Int Med 2010; 152](http://www.consort-statement.org/downloads). [↑](#footnote-ref-2)