**Definition of Clinical Trial**

NIH defines a clinical trial\* as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. (See definition below).

All NIH clinical trials are required to have appropriate Data Safety Monitoring Plans (DSMPs), approved by the PO. Please view the [NIH Policies and IC Guidance for Data and Safety](https://humansubjects.nih.gov/data_safety)  [Monitoring of Clinical Trials](https://humansubjects.nih.gov/data_safety) and the [NIA-specific data safety and monitoring policy](https://www.nia.nih.gov/research/dea/implementation-policies-human-intervention-studies).

## \*NIH Clinical Trial Definition:

[NIH Clinical Trial Definition](http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-015.html)

A research study1 in which one or more human subjects2 are prospectively assigned3 to one or more interventions4 (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.5

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1. See Common Rule definition of research at 45 CFR 46.102(d).
2. See Common Rule definition of human subject at 45 CFR 46.102(f).
3. The term “prospectively assigned” refers to a pre-defined process (e.g., randomization) specified in an approved protocol that stipulates the assignment of research subjects (individually or in clusters) to one or more arms (e.g., intervention, placebo, or other control) of a clinical trial.
4. An intervention is defined as a manipulation of the subject or subject’s environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies.
5. Health-related biomedical or behavioral outcome is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects’ biomedical or behavioral status or quality of life. Examples include: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and /or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life.

**DATA AND SAFETY MONITORING PLAN**

*Template and Guidelines*

# PREFACE

*Investigators should consider using this template when developing the Data and Safety Monitoring Plan (DSMP) for clinical studies sponsored by the National Institute on Aging (NIA).*

*Note that all instructions and explanatory text are shown in 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.*

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## PARTICIPANT SAFETY

* 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.*

Potential Risks: (*Outline potential risks for study participants*.)

**Example:** The potential risks to study participants include *(e.g., there may be temporary slight discoloration of the skin after blood draws.)*

Potential Benefits: (*Outline potential benefits for study participants*.)

**Example:** The potential benefits to study participants include *(e.g., ongoing nutritional counseling will be provided to all participants).*

## Adverse Event and Serious Adverse Event Collection and Reporting

*This section describes the procedures and timelines for adverse events (AE) and serious adverse events (SAE) collection and reporting. It should also include the definition, grading scale and “study relatedness” criteria for adverse events and specify the recipients of adverse event and serious adverse event reports (e.g., the IRB, the NIA, the Safety Officer or Data and Safety Monitoring Board).*

*Refer to the* [NIA Adverse Event and Serious Adverse Event Guidelines](http://www.nia.nih.gov/sites/default/files/niaaeandsaeguidelinesfinal12_28_07.doc) for details*.*

## Protection Against Study Risks

*This section provides information on how adverse events and other risks to participants in the study will be mediated and should specify any events that would preclude a participant from continuing with the intervention. This section should also include the informed consent procedures and measures to protect participants against risk during the study. In general, the format and content of this section are similar to the Human Subjects section of the application.*

Informed Consent Process. *Explain the informed consent process and how it will be used to protect participants.*

**Example:** The consent process informs a volunteer about the study, indicates the participation is voluntary and he/she has the right to stop at any time. Risks are enumerated in the informed consent form and described orally during the consent process.

Refer to the [Informed Consent Template](http://www.nia.nih.gov/sites/default/files/NIAInformedConsentTemplateFINAL.doc) and [Informed Consent Checklist](http://www.nia.nih.gov/sites/default/files/informed_consent_checklist_1_14_08_updated.doc) for details.

Protection Against Risks. *Describe measures to protect participants against study specific risks.*

**Example:** 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)*

## 2.0 INTERIM ANALYSIS

*This section provides information on planned interim analysis, if any, for safety or efficacy monitoring.*

**Example:** Interim analysis of the study is planned according to the alpha spending rule [Lan and DeMets]. 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 patients followed for at least six months.

*Rules for stopping the study, based on interim analysis, should also be described.*

## DATA AND SAFETY MONITORING

*This section describes who is responsible for data and safety monitoring, including names, type of information that will be reviewed and frequency of such reviews.*

*Single-site, minimal risk clinical trials and non-interventional studies can be monitored by an independent Safety Officer (SO) or the study staff if NIA deems appropriate, while more than a minimal risk single-site and all multi-site clinical trials and all Phase III clinical trials require the oversight of a Data Safety Monitoring Board (DSMB).*

**Example**: The Principal Investigator (PI) will be responsible for ensuring participants’ safety on a daily basis. The *Data and Safety Monitoring Board (DSMB)* will act in an advisory capacity to the NIA Director 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.

Refer to [**DSMB Charter**](http://www.nia.nih.gov/sites/default/files/sampledsmbcharterrevised_11_25_2011.doc) for details.

## Frequency of Data and Safety Monitoring

*This section describes the frequency of data and safety monitoring reviews.*

**Example:** The PI will be informed of serious adverse events as soon as they occur and will notify the NIA and (e.g. *DSMB*) within 24 hours of notification. The *(e.g.*

*DSMB*) will meet twice annually, either in-person or by teleconference call to review study progress, data quality, and participants safety.

Safety reports are sent to the SO twice a year and will include a detailed analysis of study progress, data and safety issues.

## Content of Data and Safety Monitoring Report

*This section describes the content of the data and safety monitoring reports.*

**Example:** The content of the data and safety monitoring report will include: (*e.g., study status, participant descriptive information, safety information, study quality*)

Refer to the [**DSMB Reports Templates**](http://www.nia.nih.gov/research/dgcg/clinical-research-study-investigators-toolbox/data-and-safety-monitoring#dsmb) for guidance.

## DSMB Membership and Affiliation

*This section includes a roster of the DSMB or the Safety Officer’s (SO) name and their affiliations.*

**Example:** The following individual(s) has/have accepted position(s) as part of the (*e.g., DSMB*). DSMB membership (safety officer) will be reviewed and approved by the NIA. Should there be any questions regarding the independence of the *DSMB*, it will be addressed and corrected if necessary at that time.

Name

Title, Organization

Name

Title, Organization Etc.

## Conflict of Interest for DSMB’s

*This section describes the conflict of interest procedure for DSMB members*.

**Example:** *DSMB members* should have no direct involvement with the study investigators or intervention. Each DSMB member will sign a Conflict of Interest Statement which includes current affiliations, if any, with 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 interests pertinent to study objectives.

## Protection of Confidentiality

*This section describes protection of data presented to the DSMB or SO.*

**Example:** Data will be presented in a blinded manner during the open sessions of the DSMB or in SO reports At DSMB meetings or in SO reports, data and discussion are confidential. Participant identities will not be known to the DSMB members or to the SO.

## DSMB Responsibilities

*The* [**DSMB Charter**](http://www.nia.nih.gov/sites/default/files/sampledsmbcharterrevised_11_25_2011.doc) *provides a detailed list of the DSMB/ SO responsibilities. They include:*

* + - Review the research protocol, informed consent documents and plans for data safety and monitoring;
		- Recommend subject recruitment be initiated after receipt of a satisfactory protocol;
		- Evaluate the progress of the trial, including periodic assessments of data quality and timeliness, recruitment, accrual and retention, participant risk versus benefit, performance of the trial sites, and other factors that can affect study outcome;
		- Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the trial;
		- Review study performance, make recommendations and assist in the resolution of problems reported by the Principal Investigator;
		- Protect the safety of the study participants;
		- Report to NIA on the safety and progress of the trial;
		- Make recommendations to the NIA and the Principal Investigator concerning continuation, termination or other modifications of the trial based on the observed beneficial or adverse effects of the treatment under study;
		- If appropriate, review interim analyses in accordance with stopping rules, which are clearly defined in advance of data analysis and have the approval of the DSMB;
		- Ensure the confidentiality of the study data and the results of monitoring; and,
		- Assist the NIA by commenting on any problems with study conduct, enrollment, sample size, and/or data collection.

## Detailed Data and Safety Monitoring Plan (DSMP) Checklist

|  |
| --- |
| **IS ITEM, IF RELEVANT, IN DSMP?** Included? |
| Ye | s No |
| **Trial Safety** |  |
|  |  |
| Potential risks and benefits for participants |  |
|  |  |
| Adverse Event and Serious Adverse Event Collection and Reporting |  |
|  |  |
| Protection Against Study Risks |  |
| **Interim Analysis** |  |
|  |  |
| Plans for interim analysis |  |
|  |  |
| Trial stopping rules |  |
| **Data and Safety Monitoring** |  |
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| Investigators’ data and safety monitoring responsibilities |  |
|  |  |
| Frequency of data and safety monitoring |  |
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| Content of data and safety monitoring report |  |
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| DSMB membership and affiliation |  |
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| Conflict of interest |  |
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| DSMB/SO responsibilities |  |

*12/19/2016 DSM Plan Checklist- Version 1.0* 1