The National Institute of Nursing Research Policy for Data and Safety Monitoring of Extramural Clinical Trials- Updated July 2026

Purpose and Scope

This policy sets forth the National Institute of Nursing Research (NINR) requirements for data and safety monitoring (DSM) for all NIH-defined clinical trials funded in whole or in part by NINR extramural programs. For each NIH-supported clinical trial, NIH requires a data and safety monitoring plan that will provide oversight and monitoring to ensure the safety of participants and the validity and integrity of the data (NOT-98-084). This policy is incorporated as part of the terms and conditions for all NINR extramural ***awards*** that include an NIH-defined clinical trial, including applicable, training, career development, research project, supplement, contract, grant, and cooperative agreement mechanisms.

Note: Per NOT-OD-26-032, Basic Experimental Studies in Humans (BESH) are not subject to the requirements under the NIH clinical trial definition.

Funding for clinical trial research activities is contingent upon compliance with this DSM policy.

This policy does not take the place of Institutional Review Board (IRB) guidelines, Food and Drug Administration (FDA) requirements, or special NIH guidelines. This policy supersedes "Policy of the NINR for NINR Data and Safety Monitoring of Clinical Trials" issued in 2019 and 2014. This revised policy is effective with competing projects issued in July FY 2026 and is effective for all future years in the competitive project periods.

Background

NIH is committed to supporting research studies that are scientifically sound and rigorously designed to operate efficiently and produce high quality, reliable scientific data to advance the NIH mission. NIH endeavors to ensure that studies are conducted safely, ethically, and in accordance with approved study plans and, as applicable, good clinical practice. In 1998 and 2000, NIH issued the NIH Data and Safety Monitoring (DSM) Policy and Further Guidance on Data and Safety Monitoring for Phase I And Phase II Trials. The DSM policy expects each NIH Institute and Center (IC) to have a system for appropriate oversight and monitoring of clinical trials to ensure the safety of participants and the validity and integrity of the data. In 2020, NIH issued the Data and Safety Monitoring Board Brief to provide clarity on the role of Data and Safety Monitoring Boards (DSMB) and the mandate for a DSMB to monitor multi-site clinical trials involving potential risk to participants. The NIH requirement for data and safety monitoring is separate and distinct from the requirement for protocol review and approval by an Institutional Review Board (IRB).

NINR Policy

All applicants and funded investigators with a clinical trial supported by NINR must provide a Data and Safety Monitoring Plan (DSMP) as part of a competing application or, in cases of delayed onset research, in a prior-approval request (See NOT-OD-15-129: Prior NIH Approval of Human Subjects Research in Active Awards Initially Submitted without Definitive Plans for Human Subjects Involvement (Delayed Onset Awards): Updated Notice).

The level of monitoring activities should be commensurate with the size and complexity of the trial, the level of risk to study participants, and phase of the trial. It is recommended that the IRB review and approve the DSMP. The monitoring activities outlined in the DSMP are to be developed with careful consideration of the relative risks to participants, the nature of the trial, and essential protections to ensure data safety. The DSMP must be reviewed and approved by NINR or the administering institute, center, or office (for awards that NINR is co-funding) before human subjects activities can begin.

Data and safety monitoring is ultimately the responsibility of the Principal Investigator (PI) or

designee and recipient institution. However, the PI as the sole Data and Safety Monitor is only appropriate for studies that *are conducted at a single site, are of minimal risk to participants, and do not include vulnerable populations*.

For most studies, data and safety monitoring may also be conducted by *independent monitoring entities external to the study team* such as an independent safety monitor (ISM), small committee (Safety Monitoring Committee (SMC), or Data and Safety Monitoring Board (DSMB). A DSMB is required for multi-site clinical trials. A DSMB is also required for Phase III clinical trials and may be required for other trials when warranted by the risk, design, population, intervention, procedures, blinding, or complexity of the study. For a single site phase I or phase II clinical trial NINR may require an independent safety monitor, safety monitoring committee, or DSMB when the trial includes high-risk interventions, high risk procedures (i.e., particularly invasive or is associated with other safety concerns), or vulnerable populations (e.g., children, pregnant women, elderly, terminally ill, or those of diminished mental capacity), blinded designs, or other factors that warrant independent monitoring. A DSMB may be established if the principal investigator, their institution or NINR deems it necessary.

The organization, responsibilities, and operation of the DSMB are mandated by NIH and NINR policy (See Appendix A: NINR Guidelines for External DSMBs). NIH's and NINR's DSMB requirements apply, regardless of whether the PI, the institution, or NINR deem the DSMB necessary."

The Data and Safety Monitoring Plan (DSMP)

The DSMP describes oversight and monitoring to ensure the safety of participants and the integrity of the data. DSMPs should address the following essential elements (see [template link] for a DSMP template that includes each of the elements below):

a. Monitoring entity (i.e., PI only, ISM, SMC, or DSMB): Describe roles, responsibilities, and expertise of everyone on the team involved in monitoring and the justification for the monitoring approach. For studies with independent monitoring entities, confirm that there are no conflicts of interest (COIs). Potential COIs for the independent monitoring entities include: 1) financial conflicts; 2) publication or collaboration with study investigators; and 3) the potential monitor is subordinate to the study investigator. If there is no independent monitor (the PI is the monitor), the plan should include a discussion of how the Institution will avert or manage any conflict of interest (COI) implicit in having the Principal Investigator as the only monitor of a clinical study. The plan should specify how COI will be ascertained and tracked.

b. Procedures for monitoring study safety which include: 1) the overall framework for safety monitoring including what information will be monitored, how information will be monitored, and by whom; 2) procedures for ensuring compliance with the study protocol, informed consent requirements, and IRB requirements (including but not limited to case audits and assessing and reporting deviations); 3) the frequency of monitoring; 4) the content of the monitoring report and timeframe for submitting the monitoring report to the independent monitor (if applicable); and 5) the timeframes for submitting monitoring meeting summaries and independent monitor recommendations and the action plan for response (if applicable).

c. Procedures for minimizing research-associated risk, including but not limited to protecting participant confidentiality and data security.

d. Procedures to ensure data quality and integrity

e. Procedures for identifying, reviewing, and reporting **adverse events (AEs), serious adverse events (SAEs)** and **unanticipated problems (UPs)** to the IRB, NINR, independent monitor (if applicable), and FDA (if applicable). Include: 1) Definitions of AEs, SAEs, and UPs; 2)

information on classification of severity, expectedness, and study relatedness; and 3) the mechanism and timeframes for reporting of AEs, SAEs, and UPs to the IRB, NINR, independent monitor (if applicable), and FDA (if applicable).
For more information see:

OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events (https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html#Q5)

NIH Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multicenter Clinical Trials (http://grants1.nih.gov/grants/guide/notice-files/not99-107.html)

Required timeframes for reporting to NINR:

- Unanticipated Problems must be reported within **5 business days** of the **PI's knowledge**.
- All adverse events that are both serious (SAE) and unexpected (i.e., have not been previously reported for the study's intervention) should be reported to the IRB, NINR, and to the independent monitor within **5 business days of the PI's knowledge** of the SAE.
- All other AEs and SAEs must be reported **at least annually with the RPPR**.

If applicable, include the type and number of events that would halt accrual and would generate a review of eligibility, monitoring, assessments, intervention, and how the resumption of accrual would occur.

f. For multi-site studies, procedures to ensure compliance with the monitoring plan and reporting requirements across study sites, role(s) and responsibility(ies) of those monitoring compliance with the DSMP across study sites, compliance monitoring timeframe, and actions to be taken if study sites are found to be non-compliant.

g. The advanced plans for interim and/or futility analysis as appropriate.

h. A plan for timely reporting of the following to NINR:

1. IRB protocol modifications corresponding with a change in risk for participants, change in scope, and/or a change in key personnel listed in the NoA. Please be advised that all changes in scope must be submitted to NINR as a prior approval request (see 8.1.2 Prior Approval Requirements) and approved by NINR prior to implementation. IRB approval of these modifications should be reported to NINR within 5 business days of IRB approval.
2. All other IRB protocol modifications should be reported annually in RPPR.
3. Notice of any actions taken by the IRB or regulatory bodies regarding the research and any responses to those actions should be reported to NINR within 5 business days of notification from IRB or regulatory body.

All personal identifiers must be removed from any documents sent to NINR.

NINR program staff will review the DSMP included with the research application prior to issuing an award. If the DSMP is insufficient, or not aligned with NINR's DSM Policy, a revised DSMP will be requested. **The DSMP must be approved by NINR before human subjects clinical trial research activities begin.** The responsibility for compliance with the DSMP rests with the PI. NINR must approve any changes to the DSMP prior to implementation.

FAQs:

1) *Does this policy apply to all award mechanisms used by NINR?*

Yes, this policy applies to all NINR-sponsored training, career, and research projects regardless of whether they are *contracts*, *grants*, or *cooperative agreements*.

2) *To what population of grants does this policy apply?*

This policy is effective with competing grants issued in or after July 2026 and is effective for all future years in the competitive project periods.

3) *My DSM plan is part of my research grant application. Is this sufficient or am I required to send something else?*

If the general DSM plan in the application is insufficient (e.g., plan is not appropriate with respect to risks of participants; essential elements are not included), the NINR will request a revised plan if your application is being considered for funding.

4) *The NINR did not request a revision of the DSM plan included in my research grant application. Does this indicate that the general DSM plan has been approved by NINR program staff?*

Yes. If you are being considered for funding, and the NINR does not request a revised DSM plan, the DSM plan submitted with the research grant application has been approved by the NINR program staff.

5) *What if the clinical trial aspect of my research begins after the first year of funding?*

This policy applies to NIH -defined clinical trials.

If the clinical trial was detailed in the application, even if it starts later, the DSMP should be included in the application.

Awards may have a restriction on the Notice of Award that human subjects clinical trial activities cannot commence until a DSMP is approved.

If the clinical trial is a delayed onset study (a clinical trial is anticipated within the period of award, but definite plans are not yet known and cannot be described in the application), the application should indicate a delayed onset clinical trial. If you are proposing a delayed onset study, please see below.

Other research activities that do not involve human subjects may proceed. See the terms and conditions of the award for further information.

6) *Where and when do I send the revised DSM plan if requested?*

All official documentation must be sent electronically to the *Grants Management Specialist*

—with a copy to the *Program Official* —listed in eRA Commons (https://commons.era.nih.gov/commons/). This documentation must be countersigned by the *Authorized Organization Representative*. The revised DSM Plan must be approved by NINR prior to implementation.

7) *If I have a Career Development (K) Award or a Training (T or F) Award do I need to comply with Data and Safety Monitoring of Clinical Trials?*

NINR Career Development awards (K awards) may support either independent clinical trials or a mentored Clinical Trial Research Experience. If the career grant awardee is carrying out an independent clinical trial, s/he should consult with his/her mentors about DSM plans for the clinical trials. Because trainees will be in a mentored stage of their career and will in most cases lack the

experience needed to provide appropriate oversight of the trial, if PI oversight is considered appropriate for the DSM plan, a senior individual responsible for monitoring the trial must be named and the role of the trainee in trial oversight should be outlined.

Career Development awards that do not include independent clinical trials, and NINR training fellowships (F) and institutional awards (T) may support studies that provide Clinical Trial Research Experience. The "Clinical Trial Research Experience" designation refers to studies where the clinical trial is led by a mentor or other investigator, with the goal of providing trainees with clinical trial experience relevant to their research interests and career goals.

While the trainee can be part of the clinical trial team and can use the data generated during the clinical trial research experience in his/her proposed research project, the Principal Investigator of the clinical trial is expected to assume overall responsibility of the trial including registering and reporting in clinicaltrials.gov, ensuring data and safety monitoring and obtaining IRB approval. NIH supported fellowships and institutional training awards do not allow the trainee to propose an independent clinical trial.

8) *What information is needed if I am proposing a pilot (delayed onset study) that was not fully described in the original application?*

If human subject studies are planned as a delayed onset study, and therefore were not adequately described in the application because they were planned for a later time within the project period ("Delayed Onset studies"),

A DSMP will be required with the description of the delayed onset project and human subjects information prior to commencement of any human subjects activities for the clinical trial.

9) *What are the requirements for DSM reporting in the annual progress report?*

The annual progress report should confirm compliance with the DSM Plan and may also contain a summary of information regarding the plan's implementation (e.g., DSMB meetings/recommendations, monitoring reports, etc.). The RPPR may also contain a list of minor protocol amendments (that are not associated with a change in scope, key personnel listed in the NoA, or risk level for participants).

While investigators can refer to other events and changes such as SAEs, major protocol changes, and DSM changes in the RPPR, the RPPR should NOT be the primary reporting mechanism for these types of information. Investigators must adhere to the reporting requirements and timelines described for these types of information above.

Appendix A

National Institute of Nursing Research (NINR) Guidelines for Extramural External Data and Safety Monitoring Board (DSMB)

DATA AND SAFETY MONITORING BOARD

a) Role of the Data and Safety Monitoring Board

The ongoing review of data by an independent review body (i.e., DSMB) assures the investigator(s) that the trial can continue without jeopardizing participant safety. These monitoring activities are distinct from the requirement for study review and approval by an IRB. Specifically, DSMBs:

1. Protect participants in clinical protocols from exposure to unreasonable or unnecessary research risks by monitoring the trial data for effectiveness and safety.
2. Review interim data in the context of the most recent scientific literature and may access unmasked data.
3. Ensure that clinical studies do not continue beyond the point when the objectives have been met and a clinically meaningful answer of importance to the scientific community and the public has been obtained.
4. Monitor study progress and conduct.

b) Responsibilities and Functions of the DSMB

The DSMB is responsible for oversight of the activities related to implementing the clinical trial to ensure participant safety, conformance to the clinical protocol, overall performance of the trial components such as the Coordinating Center and clinical sites, and integrity of the data being collected.

Since each clinical trial supported by the NINR has been approved previously by the institution's IRB, the role of the DSMB is not to serve as a peer review group to redesign any portion of the trial unless the DSMB feels that participant safety is compromised under the proposed design. In this case, the DSMB should communicate their concerns to the NINR staff and the appropriate IRB prior to the start of participant recruitment. Specific responsibilities and function of the DSMB include:

1. Have a charter that has been reviewed and approved by the board. The charter should state that DSMB members are made aware of their ability to access unmasked data and provide guidance for the timing and conditions of accessing unmasked data. The charter must be reviewed and approved by NINR prior to implementation. The charter must include a timeframe for sending Data and Safety Monitoring reports, DSMB meeting minutes, DSMB meeting summaries and recommendations, and action plans to NINR.
2. Review study protocol, plans for data and safety monitoring, including informed consent template, reporting templates for data to be presented to the board, and other items the board may wish to see before a study begins enrollment and accept or make recommendations for adjustments.
3. Establish specific guidelines for monitoring safety. This should include a listing of events that should be reported immediately to the DSMB and the

format of reporting cumulative data at intervals.

4. Review, as appropriate, interim analyses of outcome data to include allowing the unmasking of blinded data for early evidence of efficacy, lack of efficacy, or evidence of study futility.
5. Review toxicity data, such as adverse events for safety and efficacy and make recommendations as appropriate to whether the trial should continue as originally designed, be changed, suspended or terminated based on the observed beneficial or adverse effects of any of the treatments under study.
6. Review trial performance information such as participant recruitment and retention, resource center performance, and proposals for ancillary studies follow-up information and listings of protocol violations.
7. Review published reports of related studies submitted by the study investigators, or DSMB members to determine whether the monitored study needs to be changed or terminated.
8. Review proposed modifications to the study prior to their implementation (e.g., increasing target sample size, dropping an arm based on other trial outcomes or toxicity results, modifying outcomes, monitoring plans etc.) and make recommendations.
9. Review the proposed stopping guidelines as specified in the protocol and, at its discretion, recommend modification to the proposed plan, or propose a plan, if none has been proposed.
10. Provide advice and feedback on data analysis to the study statistician or study monitor.
11. As soon as possible after the meeting, and following the schedule in the charter, a written summary recommendation along with justification related to continuing, changing, or terminating the trial. In addition, provide a statement, where appropriate, concerning the impact on the trial of individually observed or cumulative adverse events.

c) Membership of DSMB

A duly constituted DSMB must have members with sufficient expertise to review the scientific design and conduct of a study, to evaluate safety and risks to participants, to interpret data statistically, and to make recommendations concerning continuation, modification, suspension, or termination of a study. Every DSMB must have an Executive Secretary who is not otherwise involved in the study or with the study team. The Executive Secretary is usually a non-voting, ex-officio member of the monitoring board with clinical trial expertise or a contractor with equivalent expertise.

The DSMB must include a **minimum of 5 voting members** that includes a Chair. Voting member composition will include at least one clinical trials expert, a biostatistician, an expert(s) in the ethics of clinical research, an expert(s) in the clinical aspects of the disease/participant population being studied, and expert(s) in the work of DSMBs. It is important that the DSMB biostatistician as well as other members have expertise in clinical trials conduct and methodology, including the work of DSMBs. At the discretion of the Chair, ad hoc members may be invited to participate for a short period of time to review specific protocols if additional expertise is desired.

d) Conflict of Interest

It is essential that voting and non-voting DSMB members do not have close current or recent affiliations with the studies they are monitoring. DSMB members should not be directly involved in protocol development, nor supervise persons who are so involved. Each proposed member will be asked to disclose potential conflicts of interest, including for example current or expected financial ties to any commercial concerns likely to be affected by the outcome of any trial. Only those individuals who provide such disclosures may serve on the DSMB. Any member directly involved with the conceptual design or analysis of a specific trial must recuse himself from all related DSMB discussions and will not receive that portion of the unmasked DSMB report. In this instance, an ad hoc member may be added to the Board for that specific trial.

1. Awardee institutions are expected to have a Conflict of Interest (COI) policy and/or plans for management and monitoring of COIs of DSMB members. This policy or plan must reflect the essentials as specified in this NINR policy. Disclosure of conflict of interest must include financial interest, professional interest (in the sense of the trial outcome benefiting the individual professionally), proprietary interest, and miscellaneous interest as described in the NIH Grants Policy and 45 CFR Part 94 and 21 CFR Part 21. Professional interest in this context is when the trial outcome would benefit the individual professionally.

RESPONSIBILITIES of SELECTED DSMB MEMBERS and PRINCIPAL INVESTIGATOR

1. Responsibilities of the DSMB Chair

a. Develops agenda

b. Chairs all meeting sessions

c. Ensures DSMB charter is finalized at first meeting

d. Ensures that meeting summaries and final minutes are adequately prepared and approved as appropriate

e. Acts as the primary contact person for the DSMB

f. Sets the meeting dates

g. Contacts new members as needed to assess their content expertise and inform them of the DSMB process

2. Responsibilities of the NINR Staff

a. Provide general advice to the PI and Executive Secretary related to DSMB operational issues according to NIH and NINR policy.

b. Attend specific sessions of the DSMB meetings at the discretion of the Chair. If invited to attend meeting by the Chair, act in the role of objective observer with no participation in deliberations or providing of additional information that may influence the recommendations of the DSMB.

3. Responsibilities of the Principal Investigator

a. Provide written reports to the DSMB on current status of the trial, interim analyses, adverse events, and problems encountered. The report may contain recommendations for consideration by the DSMB concerning clinical site performance, whether to continue accrual and/or follow up, whether to close the trial, and whether the results should be reported.

b. Amend the protocol in accordance with DSMB recommendations and notify the clinical site and IRBs as expeditiously as possible.

c. Provide to the DSMB for review modifications to the study prior to their implementation (e.g., increasing target sample size, dropping an arm based on other trial outcomes or toxicity results, modifying outcomes, monitoring plans etc.).

d. Forward DSMB reports, meeting summaries, and recommendations as appropriate to the NINR, IRB and/or other clinical research sites involved.

DATA AND SAFETY MONITORING BOARD MEETINGS

The frequency of DSMB meetings will depend on the nature of the trial. However, a DSMB should meet at least annually. Interim meetings and/or conference calls may be held at the request of DSMB members, the study leadership, the NINR Director or designee, or local IRB or awardee institution.

All meeting materials should be considered privileged by DSMB members. This confidentiality should be maintained at all times to the extent permitted by law.

Each meeting may be divided into three parts:

1. **Open Session**

   An open session at which members of the DSMB, voting and non-voting and Executive secretary, clinical trial team, and ad hoc members may be present, at the request of the DSMB Chair. The focus of the open session is on the general conduct and progress of the study. During this time, no confidential data will be discussed and the blind, if present, will be maintained.

   The PI and other appropriate study leadership and the protocol specific biostatistician should be in attendance in order to present results and respond to questions.

2. **Closed Session**

   The second part of the meeting is a closed session involving the voting members, invited ex officio members at the discretion of the DSMB Chair, and the Executive Secretary. During this part of the meeting, safety data and, if appropriate, efficacy data to include unmasking of blinded data are presented by the protocol specific statistician(s).

3. **Executive Session (may be included as part of the Closed Session)**

   The third part of the meeting involves only voting DSMB members, and the Executive Secretary, to allow the members the opportunity to discuss the general conduct of the trial, all outcome results, including toxicities and adverse events, and implications of data. The Chair may ask the Executive Secretary to not attend and the Chair will record minutes/recommendations of the session. The Chair, if applicable, may break the blind, if such action is required to make an informed decision. Recommendations will be made to continue the study as planned, to make adjustments to the study plan, suspend or to terminate the study.

   At the end of the meeting, voting members discuss and vote on these recommendations.

NINR Program Staff Attendance at DSMB Meetings:

One NINR program staff member may participate in DSMB meeting(s) at the discretion of the Chair. The Chair may decide not to invite NINR program staff if their presence may inhibit free and open discussion, or compromise or appear to compromise the board's independence. If NINR program staff are invited to participate, they should be informed of upcoming board

meetings at least 1-2 weeks in advance and receive the appropriate meeting materials at the same time as the board members. DSMB members must be informed prior to the meeting that NINR program staff are invited to the open session and, to contact the Chair if there is concern regarding NINR program staff attendance at the meeting.

NINR program staff, if invited to attend the DSMB meetings, will act in the role of objective observer and will not provide additional information that may influence the recommendations of the DSMB. NINR program staff that function as Program Officers for the study should not be privy to post-randomization data broken down by treatment group that may be discussed during the closed or executive sessions.

DATA AND SAFETY MONITORING BOARD REPORTS

a) Written Meeting Summary of DSMB Recommendations

The DSMB will issue a written meeting summary signed by the Chair and Executive Secretary that identifies topics discussed by the DSMB that describes their individual findings, overall safety assessment and recommendations with justification related to continuing, changing, suspending, or terminating the trial and the impact on the trial of individually observed or cumulative adverse events. The summary will not, however, include safety or efficacy data identified by treatment group.

1. Written meeting summaries must be submitted to NINR program staff and the local IRB within the timeline specified in the board charter and approved DSM Plan. Meeting summaries need not be sent to the NINR Director or designee unless requested.
2. In the absence of disagreement, the PI must act to implement the recommendations as expeditiously as possible regarding amending the protocol or changing the award. If the recommendations result in a change of scope for the award, NINR approval is needed prior to implementation of the recommendations. In the unlikely situation that the PI does not concur with the DSMB, then the PI will be responsible for reaching a mutually acceptable decision about the study with the local IRB.

b) Minutes of Data Safety Monitoring Board Meetings

Meeting minutes will be prepared, and a final draft version will be signed/approved by the Executive Secretary and DSMB chair. The minutes should include:

1. General highlights of the discussions
2. General recommendations
3. Action items
4. Suggested protocol/study changes and the rationale for each
5. The date for the next scheduled meeting of the DSMB should be specified at the end of the minutes.
6. Confidential data is **not** to be included in the minutes.

Final meeting minutes must be submitted to NINR program staff and the local IRB within the timeline specified in the board charter. Final minutes need not be sent to the NINR Director or designee unless requested.

RELEASE OF OUTCOME DATA

Confidential outcome data should not be made available to individuals outside of the DSMB. Any release of outcome data to individuals outside of the DSMB must be reviewed and approved by

the DSMB, and the study leadership.

Any release of outcome data to individuals outside of the DSMB must also be approved by the local IRB.

CONFIDENTIALITY PROCEDURES

No communication, either written or oral, of the deliberations or recommendations of the DSMB will be made outside of the DSMB except as provided for in these guidelines.

Outcome results are strictly confidential and must not be divulged to any non-member of the DSMB.