Data and Safety Monitoring FAQ's

National Heart, Lung, and Blood Institute
National Institutes of Health

1. **How does the NHLBI policy differ from the NIH policy?**

The NHLBI policy is aligned with the NIH policy and extends the requirement of DSM plans to include clinical research with greater than minimal risk in addition to clinical trials. The NHLBI policy explicitly requires IRB approval of the DSM plan.

2. **Who determines whether my research protocol has greater than minimal risk?**

Your IRB has primary responsibility for determination of the level of risk to study participants. When a decision is made to fund your grant or contract, the PO will issue instructions to release funds for your research protocol if the study is clearly minimal risk, as defined in 45 CFR 46.102 (i). If the PO considers your protocol to be of greater than minimal risk, an IRB-approved DSM plan will be requested. If you disagree with the PO 's assessment, you may be asked for clarification or certification of your IRB's determination of risk.

3. **Does this policy apply to all award mechanisms used by NHLBI?**

Yes, this policy applies to all NHLBI-sponsored research projects regardless of whether they are contracts, grants, or cooperative agreements. This includes, but is not limited to, activity codes including R01, R21, R34,R43,P01,F31,F32,K08,K23,U01,etc.

4. **My data and safety monitoring plan is part of my grant application. Is this sufficient, or am I required to send something else?**

NHLBI Policy requires an IRB-approved DSM plan. The DSM plan in your grant application is sufficient if (1) it contains the essential elements listed in the NHLBI policy and (2) your institutional business official documents that your IRB has reviewed and approved the relevant section of your grant application.

5. **What happens if I don't provide a DSM plan in my grant application?**

If your application is selected for funding and is either a clinical trial or clinical research entailing more than minimal risk, NHLBI will place a term and condition on the Notice of Award (NoA) restricting all human subjects research activities until the grantee can demonstrate that the IRB has reviewed and approved the DSM plan. A similar process is followed for contracts.

6. **What if the human subjects aspect of my research begins after the first year of funding?**

This policy only applies to human subjects research. For example, if the human subjects research portion of your study begins in year 3, then this policy must be followed prior to the commencement of human subjects research activities starting in year 3. Other research activities that do not involve human subjects may proceed. See the terms and conditions of the award for further information.

7. **I am concerned about protecting participants' privacy, as well as sending sensitive study data to the NHLBI PO. How should I transmit this sensitive information?**

Under no circumstances should individual patient data that has not been de-identified be sent to the NHLBI. Other sensitive or confidential aggregate data should only be sent to the ES and project staff cleared by the ES.

8. **Where and when do I send the data and safety monitoring (DSM) plan or minimal risk certification?**

If the project is a grant or cooperative agreement, all official documentation must be sent by the Authorized Organizational Representative (preferably electronically) to the GMO—with a copy to the PO —listed in eRA Commons. If the project is a contract, this documentation should be sent to the CO—with a copy to the PO —per the contract. Please send the documentation anytime after the IRB has approved the DSM plan or indicated that the research is minimal risk but BEFORE any human subjects research commences. NHLBI also should be notified if the human subjects research, DSM plan, or minimal risk designation changes during the project period.

9. **What if I cannot submit the documentation electronically?**

The documentation can be mailed or faxed to the applicable GMO or CO (see question 8 above). The following Grants Management central fax number will convert faxed documents to PDF files: (301) 451-5462.

10. **What should I do if there are changes in human subjects research risk or changes to the DSM Plan?**

Modifications to the human subjects research or DSM plan should be submitted to the NHLBI GMO or CO prior to implementation of the change in study practice. The program office should be copied on all communication.

11. **What elements should be included in communication sent to NHLBI regarding certification of IRB approval?**

    - Application grant number or contract number
    - Title of research project
    - Principal investigator (PI) name
    - Date of IRB approval or exemption
    - Appropriate signatures (e.g., IRB chair, Authorized Organizational Representative)
    - For studies with multiple protocols, the IRB identification number and approval date associated with each protocol
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12. What should I include in my annual progress report (Type 5s)?

The annual progress reports (Type 5s) should summarize the implementation of the DSM Plan, including the dates and brief description of the outcome of DSMB meetings, and PI follow-up to DSMB recommendations

13. What are the responsibilities of a Data and Safety Monitoring Board (DSMB)?

The principal role of the DSMB is to monitor regularly the data from the clinical trial, review and assess the safety and performance of its operations, safeguard the interests of study participants, and make recommendations with respect to:

- Participant Safety
- Efficacy of the study intervention
- Benefit/risk ratio of procedures and participant burden
- Selection, recruitment, and retention of participants
- Adherence to protocol requirements
- Data and Statistical Analysis plan
- Adequacy of measured and collected data
- Possible amendments to the study protocol and consent forms
- Performance of individual centers and core labs
- Impact of proposed ancillary studies and sub-studies on participant burden and overall achievement of the main study goals

14. What are the responsibilities of an Observational Study Monitoring Board (OSMB)?

The principal role of the OSMB is to monitor regularly the data from the observational study, review and assess the performance of its operations, and make recommendations with respect to:

- Performance of individual centers (including possible recommendations on actions to be taken regarding any center that performs unsatisfactorily)
- Issues related to participant safety, confidentiality, and informed consent, including notification of and referral for abnormal findings
- Adequacy of study progress in terms of recruitment, quality control, data analysis and publications
- Issues pertaining to participant burden
- Impact of proposed ancillary studies and sub-studies on participant burden and overall achievement of the main study goals

- Overall scientific directions of the study

15. What are the responsibilities of a Protocol Review Committee (PRC)?

Typically, PRCs are established for network studies that are otherwise not peer reviewed, and are tasked with assessing the scientific and design merit of each protocol including:

- Importance of the question to be addressed
- Need for multicenter network to meet objectives
- Merit of experimental design, including appropriate controls
- Availability of adequate resources, including medications
- Adequacy of patient population and number of patients, including appropriate representation of minorities and women
- Appropriate recruitment strategies
- Adequacy of proposed plans for data acquisition, transfer, management and analysis
- Adequacy of quality control of data collection and monitoring and overall coordination of protocol management
- Description of appropriate plans to train center personnel to accomplish proposed research goals
  Once protocols are finalized through the PRC process, DSMB members may still subsequently vote for approving the protocol but their responsibilities are for data quality and safety assurance.

16. When does clinical research require an independent monitoring board?

Monitoring is commensurate with risks and with the size and complexity of the trials. All intervention studies (clinical trials), regardless of the phase, must have ongoing data monitoring. The NHLBI requires data and safety monitoring boards for phase III clinical trials. For phase I and II clinical trials or other applicable clinical research, the approach to data monitoring will depend on several factors. For example, DSMBs may be appropriate if the studies have multiple clinical sites, are blinded, or employ particularly high-risk interventions or invasive or risky procedures, or are conducted in especially vulnerable populations.

Less risky clinical research and/or clinical trials that do not utilize an unhealthy or vulnerable population or are not blinded or randomized or are single-site may be suitable for safety oversight that does not include a board. These options may be safety oversight by the principal investigator in coordination with IRB and possibly local human subjects protection committee or independent safety officer. If program staff cannot determine the level of proper safety monitoring with confidence, they should consult with senior NHLBI staff including branch chief, deputy division director, and division director.

17. **How do I determine if this clinical research grant requires an institutional or NHLBI data and safety monitoring board / observational study monitoring board, or protocol review board?**

The NHLBI adds studies to existing NHLBI DSMBs or appoints NHLBI DSMBs for:

- Phase III clinical trials
- Institute-initiated clinical trials in which the scientific concept originated with NHLBI, regardless of funding mechanism, including networks and contracts
- Trials of interventions involving cell-based therapies and gene therapies
- Investigator-initiated clinical trials supported by cooperative agreements, at the discretion of the NHLBI
- Selected investigator-initiated trials with direct costs exceeding $500,000 per year, at the discretion of the NHLBI

DSMBs may be appointed by participating institutions in coordination with NHLBI program for:

- All clinical trials not cited under the section above.
- Early-phase, single-center investigator-initiated studies. The need for a DSMB will be determined by the Principal Investigator, although NHLBI program will independently evaluate the need for a DSMB by the time the monitoring plan is reviewed.

18. **Can a single person be a member or Chair of more than one board at any given time?**

The oversight of research being conducted is best served by a diversity of board participants. In general, individuals may serve on no more than two boards at any one time and may not serve as the Chair of more than one DSMB/OSMB at a time. Any exceptions must be explicitly approved by the Institute Director.

19. **What are the responsibilities of the NHLBI Executive Secretary (ES)?**

The responsibilities of the ES include:

- nomination and invitation of the Board members and Chair
- annual review of potential conflicts of interest of Board members
- assisting the Chair in setting the agenda of each meeting
- coordination of email polls and other correspondence among DSMB members between meetings
- serving as an interface between the Board and the NHLBI Program Office

- preparing minutes of all meetings and insuring their timeliness and accuracy
- In some instances, the ES may delegate some of these tasks (scheduling, note-taking, and initial drafting of minutes) to an assistant or to the Coordinating Center, but shall nevertheless remain responsible that these tasks are executed properly and on time.

20. Who can be an NHLBI ES?

The NHLBI ES will be chosen by the NHLBI Division Director and can be any staff member whom the Director feels can perform the task well and without a real or apparent conflict. The Institute statisticians who attend the DSMB/OSMB meetings are often considered to be part of the project office and therefore would not usually serve as Executive Secretary. For specific DSMBs covered by an external contract, the contractor may provide the ES as part of its scope of work. In such cases, the NHLBI will appoint a staff member as a liaison.

21. What is the role of the NHLBI Program Official (PO)?

The PO is the NIH official responsible for the programmatic, scientific, and/or technical aspects of a grant or cooperative agreement that involves normal program stewardship of the award.

PO responsibilities may include the following activities:

- Enforcement of general statutory, regulatory, or policy requirements;
- Approval of awardee plans prior to award and review of performance after completion;
- Evaluation of progress by reviews of technical or fiscal reports, site visits, or external consultants, to determine that performance is consistent with the terms and conditions of the award;
- Technical assistance requested by awardees, or unanticipated procedures to correct programmatic or financial deficiencies in awardees' performance;
- Scientific/technical discussions with awardees, or actions to facilitate or expedite interactions between awardees, e.g., organizing and holding meetings of investigators.

22. What is the role of the NHLBI PO with respect to participation in the DSMB/OSMB?

The PO should be easily accessible should questions arise during DSMB/OSMB meetings.

23. What is the role of an NHLBI Project Scientist?

The Project Scientist is a person with substantial scientific involvement in a given study.

Substantial scientific involvement may include the following activities:

- Cooperation or coordination with, or assistance to, awardees in performing project activities, e.g., development of research protocols; data collection,

analyses, and interpretations; re-establishment of objectives during the course of a project; or holding FDA Investigational New Drugs (INDs) for investigational drugs;

- Providing for an option to halt a project activity if technical performance requirements are not met or if program objectives have already been met;
- Specifying under the terms and conditions of award that the project be structured in stages and that NIH staff review and approve each stage before work may begin on such stage, e.g. concepts for research projects;
- Assistance with the selection of contractors or sub-awardees under the assistance award, and in the selection of key project personnel other than principal investigators of projects or sub-projects;
- Technical monitoring to permit specific direction of the project, including recommending approval of changes in experimental approaches;
- Participation on committees (other than peer review, see below) as a voting member as needed (the chairperson will be someone other than an IC staff member) or in other functions responsible for helping to guide the course of long-term projects or activities; and
- Participation in the presentation of research results, including publications from the project;

24. If a DSMB/OSMB oversees more than one study, will there be a separate ES for each study?

No. The ES of the DSMB/OSMB will serve in this capacity for all the studies assigned to the board.

25. What is the purpose of an Executive Session?

The purpose of the Executive Session is to permit the DSMB to consider sensitive issues and discuss recommendations privately, without anyone from the program (or even the ES, if they so choose) in the room. This helps insure their complete independence for making decisions and formulating recommendations.

26. Under what circumstances might someone be invited to a DSMB - Closed Session?

The following additional NHLBI staff representatives may attend the Closed Session with the approval of the program official in consultation with the executive secretary and the DSMB Chair:

- Junior staff for purpose of training or mentoring;
- Staff with particular expertise related to a given study; and,

- Senior NHLBI Staff, i.e. the Institute Director, Division Directors, Associate Director.