National Institute on Alcohol Abuse and Alcoholism

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In this Section

NIAAA Data and Safety Monitoring Plan Requirements for NIAAA-funded Clinical Trials

Purpose

To provide grant applicants with guidance and information on the development of data and safety monitoring plans (DSMP) for NIH-defined clinical trials funded by the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

Introduction

In June 1998, the National Institutes of Health (NIH) issued a policy on data and safety monitoring requiring oversight and monitoring of all NIH funded clinical trials. This monitoring is to be commensurate with the risks, nature, size, and complexity of the trial. For purposes of this policy, 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. Interventions 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. Clinical trials are also used to determine whether new interventions are safe, efficacious and effective, and to evaluate the effects or impact of particular biomedical or behavioral interventions. In June 2000, the NIH issued further guidance on data and safety monitoring for phase I and phase II trials.

The NIAAA policy on data and safety oversight fulfills this mandate by ensuring that an appropriate monitoring structure is in place for all NIAAA-supported clinical trials (e.g., grants, contracts and cooperative agreements) and that NIAAA is informed in a timely manner of all recommendations that derive from monitoring activities. This policy is not intended to usurp the role of the local Institutional Review Board (IRB) or other regulatory and monitoring entities (e.g., Food and Drug Administration). Release of funds for clinical trials is dependent upon compliance with this policy.

Data and Safety Monitoring Plan

Applicant organizations that plan to conduct a clinical trial must include a DSMP in its entirety as part of the application submission process. During review, the peer review group (e.g., Scientific Review Group) will evaluate the DSMP and any comments or concerns will be communicated to the potential contractor or grantee within the summary statement

critique(s). The DSMP must be approved by the NIAAA Project Officer (PO) (for grants and cooperative agreements) or, for contracts, the NIAAA Contracting Officer's Representative (COR) prior to release of the Notice of Award. After review and approval of the DSMP by NIAAA, investigators shall not modify the DSMP without additional prior NIAAA review and approval from the PO or COR.

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. Below is a listing of what, at a minimum, should be included in the DSMP.

At a minimum, the DSMP must include the following critical elements:

1. Description of the entity(ies) responsible for monitoring the trial (e.g., an independent monitoring person or group, the Principal Investigator (PI), the study physician (if different from the PI), a Data and Safety Monitoring Board [DSMB], etc.) and procedures for monitoring subject safety. *Note: Phase III clinical trials must have an independent DSMB. Phase I and II studies that either involve multiple clinical sites, use high risk interventions, or involve vulnerable research participants may require a DSMB at the discretion of NIAAA.*
2. Name of the responsible party (e.g. PI, study physician if different from the PI) who will distinguish a serious adverse event (SAE)[1] from a non-serious adverse event (AE) and provide attributions (causality and severity). PIs must indicate that SAEs, AEs, and unanticipated problems will be managed consistent with their local IRB guidelines.
3. Describe the follow-up plans for SAE and unanticipated problems.
4. Risks associated with study participation.
5. Safety Reporting
    1. SAEs and unanticipated events which are considered "at least possibly related" during the treatment and follow-up phases must be reported to the local IRB and to the NIAAA project officer within 48 hours of knowledge of the SAE. All other SAEs and unanticipated events must be reported within the time period mandated by the local IRB.
    2. Annual report summarizing all AEs must be provided to the NIAAA PO. The annual report should include:

        i. confirmation of adherence to the data and safety monitoring plan;

        ii. a summary of any data and safety monitoring issues that occurred since the previous reporting period;

        iii. a description of any changes in the research protocol or the data and safety monitoring plan that either does or potentially affect risk;

        iv. all new and continuing IRB approvals.
6. Inclusion/exclusion criteria[2]
7. Assurance that trained personnel will be present or on call when specific study procedures take place, based on the level of risk and consistent with approved protocol, policies and guidance from the local IRB and/or other regulatory and monitoring entities. Examples include (but are not limited to) the administration of alcohol, other drugs and/or medications; invasive or other study procedures or testing; etc. The types of trained personnel (e.g.: nurse, nurse practitioner, physician assistant, physician, etc.) should be stated.
8. For studies in which alcohol is administered, assure that NIAAA guidelines for the administration of alcohol will be followed. These guidelines can be found here: Alcohol Administration Human Laboratory Studies.
9. Specific plan for referral to treatment during follow-up phases for any research participant who requires additional intervention due to significantly increased alcohol consumption or serious psychiatric/medical symptoms.
10. Procedures for data quality assurance and protecting confidentiality of participant data (e.g., Certificate of Confidentiality).
11. Include certification of IRB approval(s) of the study protocol. Approvals should be submitted (preferably electronically) to the NIAAA Grants Management Officer (GMO) before initiating a proposed clinical trial. For multi-site studies, the Data Coordinating Center (DCC) and associated study sites must submit certification of IRB approval as well as assurance that IRB approvals have been obtained for all study sites, are on file at the clinical site and DCC, and are available to the NIAAA upon request.
12. Analysis plan including the power calculation(s) to demonstrate clinical efficacy. There should be discussion of any planned interim and/or futility analyses, including adjustments for allocating "alpha" on "multiple looks" at the data.
13. Stopping rules for clinical trials (if applicable). Generally, stopping rules reflect one of the following conditions: 1) there is clear evidence of harm; 2) there is no likelihood of demonstrating treatment benefit (futility); 3) there is overwhelming evidence of the benefit of treatment.

For questions or comments please contact:

Megan Ryan
Clinical Program Manager
Division of Medications Development
(email) mryan1@mail.nih.gov
(phone) 301-443-4225

[1] *Serious Adverse Events* include adverse events that result in death, require either inpatient hospitalization or the prolongation of hospitalization, are life-threatening, result in a persistent or significant disability/incapacity or result in a congenital anomaly/birth defect. Other important medical events, based upon appropriate medical judgment, may also be considered Serious Adverse Events if a trial participant's health is at risk and intervention is required to prevent an outcome mentioned. https://grants.nih.gov/clinicaltrials_fdaaa/definitions.htm

[2] Specify that female subjects who are pregnant, nursing, or not using effective methods of birth control will be excluded from studies involving the administration of alcohol and/or drugs.
