Introduction

The purpose of the NIDA Clinical Trials Network (CTN) is to conduct large multi-site drug abuse clinical trials to determine the effectiveness of drug abuse/addiction interventions across a broad range of treatment settings and patient populations. An essential part of this process is to adequately monitor the safety of participants in the studies to assure the continuing acceptability of the risks to subjects who participate in these trials.

CTN Policies for Safety Monitoring of Intervention Studies

1. Appropriate safety monitoring will be included in all studies conducted under the auspices of the NIDA Clinical Trials Network.

2. All CTN studies must adhere to current NIH policies concerning the conduct of clinical trials and applicable regulatory requirements.

3. All CTN studies must be monitored by a Data and Safety Monitoring Board (DSMB).

4. The Principal Investigator at each Node is responsible for assuring the safety of study participants in the Community Treatment Programs in their Node and ensuring that local Institutional Review Board(s) are fully informed of safety issues that may arise throughout the CTN for studies conducted at that Node.

5. Medical officers at NIDA are responsible for evaluating, monitoring, and reporting to the NIDA CTN Office on the safety of study participants in all studies conducted under the auspices of the CTN.

6. All serious adverse events[1] (SAE) will be monitored and tracked according to NIDA and FDA guidelines (see below).

7. Responsibility for compliance with FDA regulations for studies conducted under IND will be determined by who holds the IND.

NIH policies

As the sponsor of the CTN, NIDA has specific obligations for monitoring the safety of participants in CTN trials. In particular:

[1] Note that the FDA definition of adverse events is commonly understood to involve pharmacotherapy. However, the definition of Serious adverse event in this context (i.e., an event resulting in Death, a life threatening event, an event resulting in hospitalization, prolongation of hospitalization, disability or birth defect/congenital anomaly) can be applied equally to any adverse event in any clinical trial, including studies of behavioral interventions. The term serious adverse event is used in this broader sense in this policy.

It is the policy of NIH that all phase III trials conducted or sponsored by NIH will be monitored by an Independent Data and Safety Monitoring Board. Both studies of behavioral interventions and pharmacotherapies require monitoring by a DSMB.

In order to fulfill this responsibility a NIDA medical officer is responsible for evaluating data concerning the safety of the interventions being evaluated in CTN studies. In addition, NIDA has established an Independent Data and Safety Monitoring Board to monitor CTN studies, and requires the expedited reporting of Serious Adverse Events to NIDA.

NIDA-CTN Data and Safety Monitoring Board (DSMB)

The DSMB is an independent board including experts in addictions treatment, clinical trial design and ethics. The DSMB is appointed by and reports to NIDA. This Board monitors the conduct of all CTN clinical trials to ensure the safety of participants and the validity and integrity of the data collected at participating clinics. The DSMB also may make independent assessments of treatment effectiveness and whether a trial should continue by reviewing data accrued by the CTN and other applicable information.

The DSMB operates according to standard procedures approved by the Director of NIDA. These procedures are included as an appendix to this document. These procedures comply with and will be revised according to:

1) NIH policy requiring all phase III clinical trials sponsored by NIH to be monitored by a DSMB.

2) Current GCP Standards, as described in FDA consolidated guidance on Good Clinical Practices, ICH E6.

3) FDA Guidance on Statistical Principles for Clinical Trials, ICH E9.

These procedures are intended to ensure an independent and confidential review of accruing clinical trial data from the CTN.

Expedited Reporting Of Serious Adverse Events In the CTN

In order to assure effective safety monitoring in CTN studies the following policies will apply to all trials conducted by the CTN:

1) All adverse events occurring during a CTN clinical trial and meeting the FDA definition of “Serious” will be reported to the Lead Investigator and to the NIDA CTN Office in an expedited manner[2].

[2] Note that the requirement for expedited reporting:

2) All subjects who experience serious adverse events will be followed until resolution of the serious adverse event is known.

3) All Serious Adverse Events reported from CTN trials will have a written evaluation of their medical significance prepared by the responsible NIDA medical officer. This report will include assessment of the event reported along with any recommendations for actions to protect the safety of study subjects, or meet applicable regulatory requirements. Recommendations might include, for example, convening a special meeting of the DSMB or submission of an IND safety report to FDA.

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a) Applies regardless of the investigator's assessment of the relatedness of the Serious Adverse Event to the intervention under study or the severity or resolution of the event.
b) Applies equally to pharmacotherapy and behavioral therapy trials.
c) Applies equally to trials requiring an IND and those not requiring an IND.
d) Applies to all Serious Adverse Events occurring during a trial, including those events that may occur during any post-treatment observation period as defined by the protocol.
e) Applies to drug overdoses which meet the definition of serious (e.g. require hospitalization)
f) Applies to suicide or suicidal behavior causing a serious adverse event in the subject (e.g., hospitalization)