Data and Safety Monitoring for Clinical Trials – NINDS

Robin Conwit, M.D.
Program Director, Division of Clinical Research
National Institutes of Neurological Disorders and Stroke

*Recommendations for data monitoring committees from the Clinical Trials Transformation Initiative, Calis and Lewis, et al. Clinical Trials, 2017.

Disclosures

No commercial or financial interests, relationships, activities, or other conflicts of interest to disclose.

This presentation will not include information on unlabeled use of any commercial products or investigational use that is not yet approved for any purpose.

Mandated by NIH

- **NIH-sponsored clinical trial monitoring activities governed by nature, size, and complexity of the trial**
- **DSMB mandated for:**
  - All Phase III studies + masked Phase I/II therapeutic studies
  - Any high risk Phase I or II clinical trial
- **NINDS requires that all clinical trials involving interventions with more than minimal risk to participants have additional safety monitoring.**

Roles of a DSMB or Safety Officer

- **Ongoing review of the data by an independent individual (Safety Officer) or committee (DSMB)**
  - Assures trial can continue without jeopardizing patient safety
  - Ensures trial conducted according to the highest scientific and ethical standards
  - Ensures high quality, validity and scientific integrity of the study results
  - Assists in determining if any of the treatment procedures practiced should be altered or stopped

NINDS Responsibilities

- **Reporting Structure - DSMB members report only to NIH**
- **NINDS is Responsible for oversight of data and safety monitoring to ensure:**
  - safety and quality assurance is in place and is appropriate for study
  - monitoring is timely and effective

  Must have appropriate expertise to inform
  - the Institute of recommendations emanating from monitoring activities

DSMB Membership

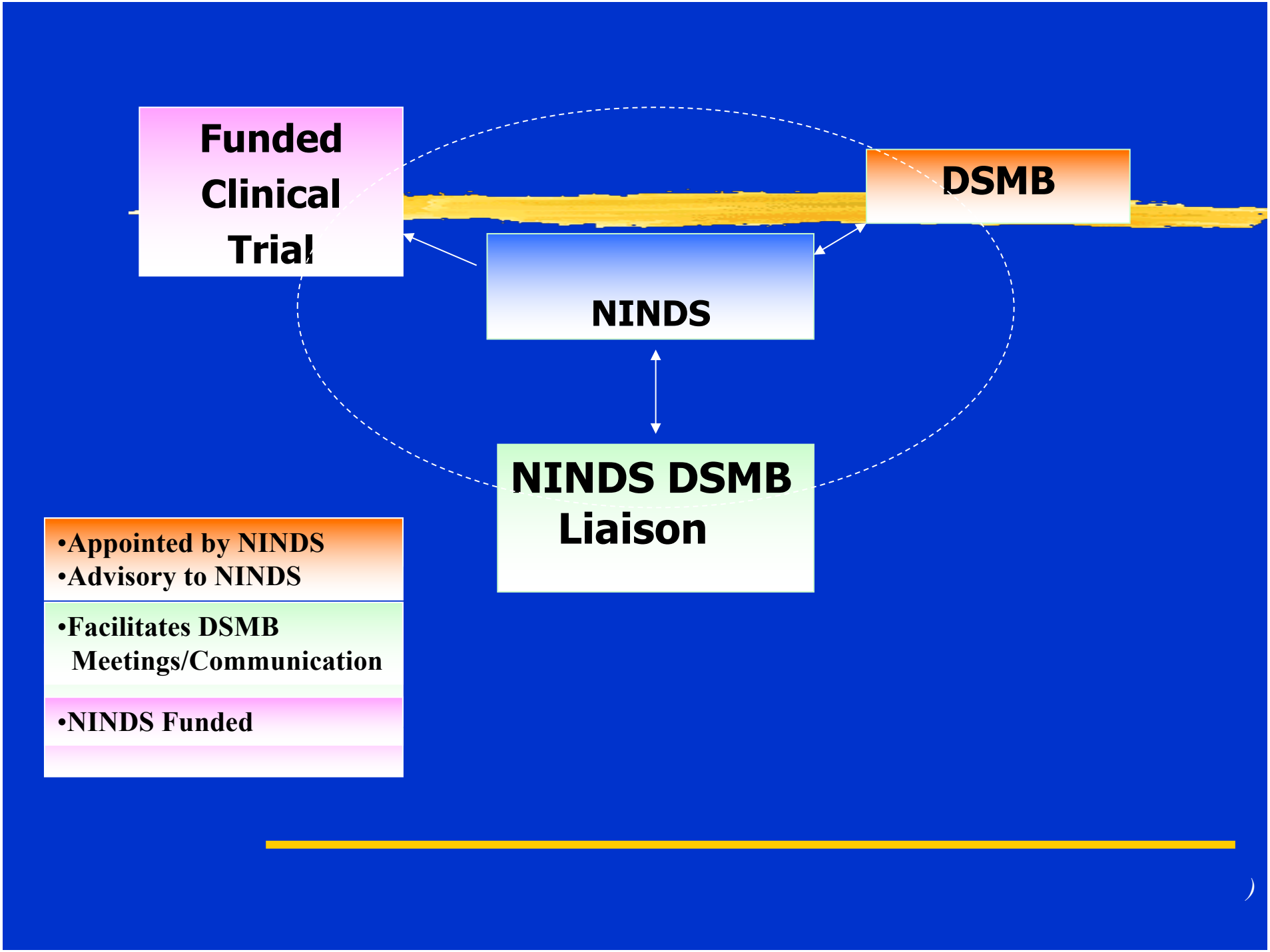
- **NINDS appoints members to the DSMB**
  - Voting members should have appropriate expertise in the relevant scientific and methodological areas
  - Members are likely to be clinicians, methodologists, statisticians, laboratory scientists, ethicists and patient advocates
- **Members must be completely independent of the investigators and must have no financial, scientific, or other conflict of interest with the trial**
- **Members must attest to absence of conflict of interest in writing**

Safety Officer

- **In small, single-site studies, safety monitoring is often performed by a statistician in conjunction with a Safety Officer. The Safety Officer is:**
  - Appointed by the grantee institution
  - Reviews adverse events (AEs) and Serious Adverse Events (SAEs) on an ongoing basis to determine action, if needed

Independent Medical Monitor

- For NINDS-sponsored studies which are likely to entail risks, an Independent Medical Monitor is often appointed to review serious adverse events in "real time"
- May be in addition to a DSMB
- For NINDS trials, we will specify appropriate level of safety monitoring


Funded Clinical Trial
DSMB
NINDS
NINDS DSMB Liaison
•Appointed by NINDS
•Advisory to NINDS
•Facilitates DSMB Meetings/Communication
•NINDS Funded

DSMB Activities

- **Data and safety monitoring activities focus on several areas and members review:**
  - Performance Data – patient recruitment/ retention/drop-out rates
  - Safety Reports
  - Treatment Monitoring
  - Interim Analysis
  - Stopping rules

DSMB Activities *continued*

- **DSMB members are also responsible for:**
  - Protection of the confidentiality of the trial data
  - Recommending to NINDS whether to continue or conclude the trial
  - Monitoring patient recruitment and retention rates to ensure end goals for recruitment will be met.

DSMB Authority

- **The DSMB can:**
  - Request to see all blinded and unblinded/masked and unmasked data
  - Request reports
  - Advise the Institute to start, stop or modify a trial protocol

DSMB Meeting Design

- **General Open Session Discussion Items**
  - patient accrual
  - compliance with protocol
  - problems encountered
  - Data is BLINDED
- **Closed Session Discussion Items**
  - UNBLINDED safety and efficacy data
  - confidentiality of data
  - Advise NINDS to start, stop or modify a trial protocol

DSMB Meeting Flow

- **Closed Executive Session**
  - DSMB members, NINDS DSMB Liaison
- **General (open) Session**
  - Coordinating Center, Principal Investigators and institution staff, DSMB members, NINDS DSMB Liaison, NINDS Program Director
- **Closed Executive Session**
  - DSMB members, Study statistician, NINDS DSMB Liaison
- **Open Session**
  - Principle Investigators, DSMB members, NINDS Program Director, NINDS DSMB Liaison

DSMB Process

- **First organizational meeting, prior to trial initiation**
  - Discuss protocol
  - Establish monitoring guidelines
- **Bi-Annual Meetings**
  - Via conference call and/or face-to-face
    - Review accumulating safety data
    - Conduct pre-specified interim analysis
- **Emergency meeting may be called by the DSMB or NINDS at any time should patient safety issues arise!**

Case Studies